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DIABETES MELLITUS.[1]

By EWEN DOWNIE, M.D. (Melbourne), M.R.C.P. (London),
Honorary Physician to Out-Patients and Officer in Charge of the Diabetic Clinic, Alfred Hospital, Melbourne.

Insulin and Vital Statistics.

SINCE the isolation of insulin in 1922 a remarkable change has taken place in our attitude to *diabetes mellitus*; much knowledge has been gained, many of our earlier ideas of treatment have been radically altered, the prognosis has been modified and knowledge of sequelæ increased, but the cause and cure of the disease, if it be a single disease, remain unknown.

[1] Read at a meeting of the Victorian Branch of the British Medical Association on July 6, 1938.

The whole outlook on life for the sufferers from this complaint has changed. The diabetic child of today is living, growing and developing in a fashion closely approximating to normal, and the diabetic adult can be restored to reasonable health and may become a useful member of society, capable of taking his place in the community. In the past fifteen years many patients have been brought safely through serious illnesses and major surgical procedures, and the dread of diabetic coma has been greatly reduced.

Although these facts are beyond question, it would appear at first sight, if we turn to vital statistics, that little if any alteration has taken place, as the figures of diabetic mortality throughout the world reveal the death rate from diabetes to be increasing. This has been used by those opposed to insulin therapy as an argument to discredit its value. However, it must be obvious that

insulin, a palliative measure in the treatment of an incurable disease, cannot influence the mortality if the incidence remains the same. If the incidence should increase, then the mortality must also increase, although with improvement in treatment the expectation of life may be prolonged. That is, in fact, what is happening. Furthermore, this increase appears to be taking place mainly amongst middle-aged females.

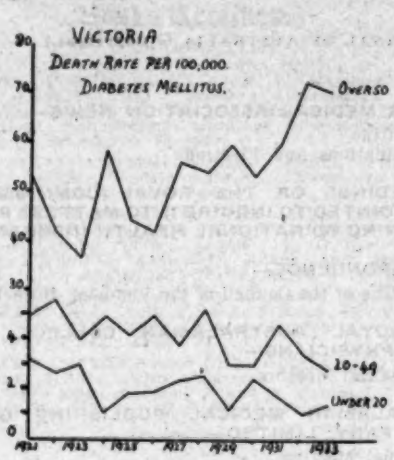

FIGURE I.

A closer study of vital statistics will indicate the real effect of modern treatment. Thus, in Figures I and II it is apparent that in Victoria the

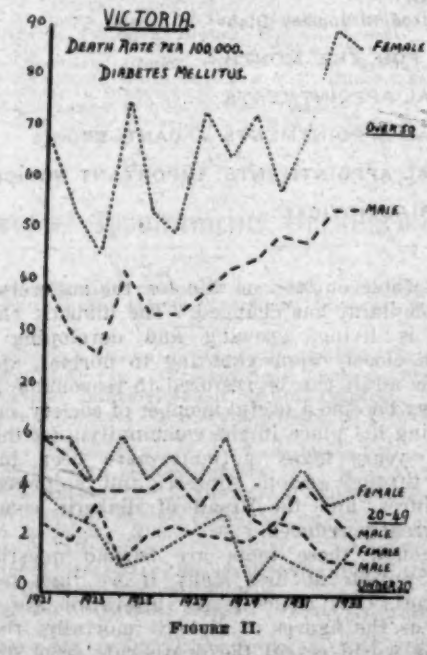

FIGURE II.

death rate from diabetes is declining in the age-groups under fifty years, but this alteration is overshadowed by an increase in the death rate over fifty years. If these figures are considered according to the mortality in the two sexes at various age-periods it will be seen that there is a very close correspondence between the male and female deaths before the age of fifty years, and that the rate of decline is approximately the same. Over the age of fifty years the death rate of females is greater than that of males and appears to be increasing more rapidly. The effects of modern treatment upon diabetic mortality can be shown in yet another way; if the deaths from the disease in a certain period of time be considered as 100, then the deaths occurring during the various age-periods can be expressed as percentages. In Figure III the mortality from diabetes in Victoria from 1920 to 1933 is set out in this fashion. It is quite obvious that there has been a considerable fall in percentage in the earlier age-groups and that the maximum has moved from the age-group 60 to 65 to that of 70 to 75 (Figures III and IV).

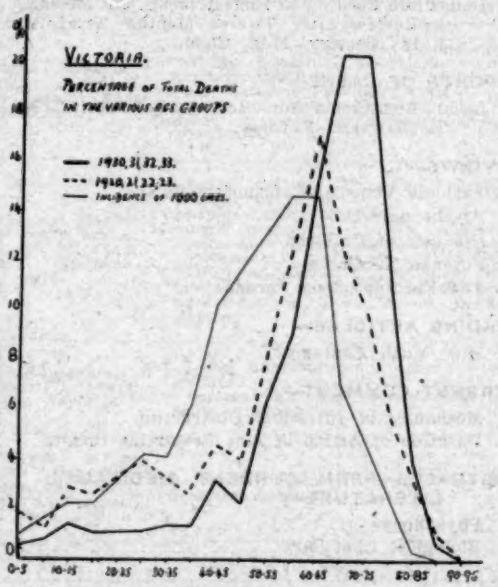

FIGURE III.

The improvement can be summarized thus: There has been a definite decrease in the number of deaths from diabetes, of both males and females, before the age of fifty years, and there has been a decided increase in the number of deaths after that age since the introduction of insulin. And on theoretical grounds this is what is to be expected in the trend of mortality of any incurable disease after the introduction of some new treatment which, although not curative, possesses the property of prolonging life.

Ætiology of Diabetes.

The first experimental pancreatectomy was performed some 250 years ago by Brünner; but his observations passed unnoticed. It was not until Minkowski, in 1889, showed that removal of the pancreas of a dog resulted in a condition indistinguishable from *diabetes mellitus* in man

that attention was first directed to the pancreas. Within recent years, however, the pancreatic theory of origin has been shown to be inadequate to explain many of the observed clinical and experimental facts. Without any attempt to traverse the subject of recent research, attention can be directed to certain outstanding discoveries. Twelve years ago, on histological grounds, Warren indicated that probably in some cases at least the pancreas was not primarily at fault. It was his experience that in a number of fatal cases the histological changes in the pancreas were not so marked as they were in patients who died from other causes, never having shown evidence of diabetes during life. Himsworth, a few years ago, propounded an interesting theory that insulin was an inert substance requiring activation by some unknown kinase. In his opinion, this substance, if not present in adequate amounts, could cause a defective utilization of insulin, with consequent development of a diabetic syndrome.

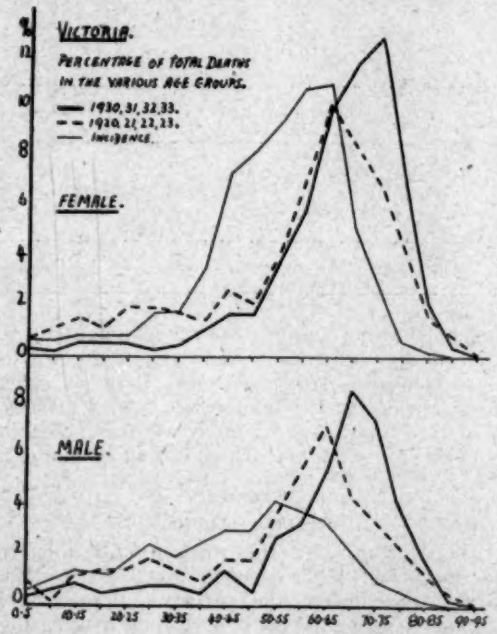

FIGURE IV.

Another new conception of *diabetes mellitus* developed from the work of Houssay and his colleagues. Houssay's original experiments indicated that removal of both the pancreas and the pituitary gland of an animal was followed by a milder type of diabetes than that which occurred when the pancreas alone was removed. About the same time the work of Collip and his school showed the extraordinary influence exerted upon the whole endocrine system by the pituitary gland. They isolated numerous hormones from the anterior lobe of the pituitary; one of these appears to have the property of acting as an antagonist to insulin. It is still unknown whether this diabetogenic hormone is identical with or is closely allied to prolactin, the anterior pituitary hormone responsible for lactation. Attention has also been directed to the influence of the adrenal cortex upon experimentally induced diabetes; but this work has not yet progressed sufficiently far to permit of any dogmatic statements. C. N. H. Long, in concluding a lecture to the Harvey Society of New York during 1937, indicated the trend of modern opinion by the following remarks:

> . . . enough, however, has been discussed to demonstrate that the endocrine control of metabolism is far more complex than appeared possible a few years ago. . . . Diabetes mellitus is perhaps the one most immediately affected by this new knowledge. In the future we must cease to focus our interest upon the pancreas as the sole determinant in this disorder, but widen it to include extra pancreatic factors known and unknown.

Another unexplained observation regarding the incidence of this disease is the influence of heredity. Priscilla White, on a basis of sound reasoning, has shown that diabetes is inherited as a Mendelian recessive characteristic.

It is difficult to correlate these experimental observations with clinical facts. However, the gross difference in the picture presented by the acute wasting and fatal complaint in adolescence when compared with the insidious and at times unrecognized condition in elderly people arouses the reflection that these diseases, although presenting certain common features, may not be identical. When the extraordinary complexity of the processes which are concerned with the digestion, absorption, storage and utilization of carbohydrates is considered, it is not reasonable to suppose that the fault must always lie in a failure of the pancreas to produce insulin. Thus you will see that at the present time the ætiology of diabetes is lost in a maze of unexplained and to some extent contradictory facts. The position is further confused because the same principles of treatment, if used intelligently, yield satisfactory results when applied to most sufferers from the disease.

Symptoms.

The symptoms of diabetes are variable. Generally speaking the earlier in life the disorder develops, the more sudden is its onset, and the diabetes of young persons is usually more severe than that of the middle-aged. However, to both of these statements exceptions are to be found. Everyone is familiar with the typical history of an acute case, with the sudden development of excessive thirst, polyuria and the rapid loss of body weight and strength. Such a patient, if untreated, may progress to coma within a few weeks or months. The more common picture is that of diabetes in middle life, when the onset is often quite insidious, such as by a previous obesity followed by some loss of weight, usually not great, together with lassitude and tiredness. Again, so quietly may it develop that attention is first directed to one of its complications, such as *pruritus vulvæ*, retinitis or gangrene. I would stress the importance of treating such patients as strictly as one would the

TABLE I.

Tabular Record of a Male Patient, aged Forty-seven Years in 1936.

Date.	Remarks.	Results of Glucose Tolerance Test, showing Percentage of Blood Sugar.				
		Fasting.	Half an Hour after Glucose.	One Hour after Glucose.	One and a Half Hours after Glucose.	Two Hours after Glucose.
1915	Glycosuria. Qualitative restriction of diet	—	—	—	—	—
1926	Carbuncles. Diet restricted as to carbohydrates and rich in fats. This was continued till January 7, 1936 ..	—	—	—	—	—
1930		0·06	0·13	0·17	0·18	0·15
1931		0·09	0·16	0·22	0·23	0·17
1932		0·08	0·13	0·14	0·16	0·16
1933		0·07	0·16	0·20	0·18	0·16
1934		0·08	0·20	0·18	0·15	0·15
1935		0·08	0·15	0·18	0·18	0·14
January 13, 1936	Diet changed on January 7, 1936, to consist of 200 grammes of carbohydrate, 95 grammes of protein and 100 grammes of fat a day	0·10	0·18	0·23	0·18	0·11
April 4, 1936 ..		0·09	0·17	0·20	0·12	0·09

acute, adolescent type. The effects of uncontrolled diabetes in middle and later life are very serious, and although the sequelæ are in part preventible, when once developed they are incurable.

Diagnosis.

The diagnosis is usually obvious when glycosuria occurs in conjunction with a sudden history of thirst, polyuria and loss of weight. However, it is never wise to assume the existence of diabetes without seeking confirmation by blood sugar analysis. In milder cases and cases of symptomless glycosuria this investigation is essential, as it is quite impossible to make a diagnosis by history and urine examination alone. The attitude of neglecting glycosuria because it is slight in amount or inconstant in its appearance cannot be too strongly deprecated.

I do not propose to discuss the details of blood sugar analysis, but would point out the influence which the previous dietary habits of a patient may have upon the type of curve obtained. To interpret properly the results of such a test due consideration must be given to this fact. An extreme example is the observation that a normal adult, in whom there has been induced an artificial state of ketosis by carbohydrate starvation, will very often give a result of a glucose tolerance test which is identical with that obtained in a case of true diabetes. Another important diagnostic point is the recognition of the fact that carbohydrate metabolism is disturbed by infections and by pregnancy. A glucose tolerance test performed in such circumstances, if the result is abnormal, should always be repeated in three to six months' time before the diagnosis of *diabetes mellitus* is finally made.

Treatment.

General Considerations.

Diabetes is an incurable disease, and when it is once diagnosed its treatment usually involves a radical alteration in the patient's dietary habits. He must be provided with a scheme of treatment, namely, a regulated diet and possibly insulin therapy, which should be such that it will keep the urine constantly sugar free and will enable him to work and maintain his weight at a satisfactory level. The management of diabetes does not end with this; the patient must be educated in the way he should live; he must know how to vary the diet to avoid monotony and how to judge his meals when away from home. In my opinion, this education of a patient is just as important as the actual regulation of the diabetic conditions. The patient must understand the reasons underlying his treatment and the penalties of neglect if it is not carried out.

I shall not deal with the principles underlying the formulation of diets, but shall proceed to the manner of dealing with certain typical cases. When

TABLE II.

Record of Patient E.S., Aged Forty-one Years, showing Influence of Infection on Carbohydrate Metabolism.

Date.	Remarks.	Results of Glucose Tolerance Test, showing Percentage of Blood Sugar.				
		Fasting.	Half an Hour after Glucose.	One Hour after Glucose.	One and a Half Hours after Glucose.	Two Hours after Glucose.
July, 1936 ..	Glycosuria discovered at routine examination prior to operation for gall-stones. Stabilized on a diet of 100 grammes of carbohydrate, 70 grammes of protein and 100 grammes of fat and 10 units of insulin before breakfast and the evening meal. (Insulin was discontinued after four weeks)	—	—	—	—	—
August 6, 1936		0·12	0·19	0·21	0·20	0·19
February 10, 1937		0·09	0·17	0·20	0·14	0·11
May 19, 1937 ..	Dietary restrictions had been removed ..	0·10	0·17	0·16	0·11	0·11
October 27, 1937		0·09	0·13	0·11	0·08	0·08
June 1, 1938 ..		0·10	0·16	0·14	0·09	0·08

one is confronted with an untreated diabetic patient, what procedure is to be adopted? If circumstances permit, the patient should be admitted to hospital for a few weeks; the reason for this being that it is then possible to get him under control in a much shorter space of time than if he remains at home away from supervision and without proper instruction in the weighing of food and testing of urine. For patients requiring insulin I would state that a period of hospital instruction is essential. Surely, if a patient is expected to control his disease for the rest of his life, a short period of schooling in the proper methods is not a waste of time. My own practice is never to put such patients to bed unless it is necessary because of some complication. On the contrary, I endeavour to keep the patient at work, using the hospital as a boarding-house; for in this way I can plan his diet for his ordinary daily life and not for a set of artificial conditions. I find that I thus obtain much greater cooperation from the patient.

The method of commencing treatment is largely a matter of experience. There are certain patients in whom the severity of the symptoms makes it obvious that insulin will be required. On the other hand, there are milder cases in which it is likely that dietary restriction alone will suffice to control the condition. There is also an intermediate group of patients to whom it is wise to give a trial of dietary treatment, and, if after a short period of observation no improvement is noticed, insulin treatment should be commenced.

In the case of a young adult who has lost one or two stone in weight within two or three months, who is feeling tired and weak, looks wasted and whose urine contains a quantity of acetone, there is, in my opinion, no purpose in starving or underfeeding him because it is certain that insulin will be required for his control. It is my practice to commence feeding such a patient well from the beginning of treatment. It does not matter whether some organized plan of diet, such as the line-ration scheme, is used, or whether a special diet is calculated; the patient should be given a sufficient caloric intake to enable him to regain his weight and strength. If reliance is placed upon arbitary figures of 25 or 30 calories per kilogram of body weight, it is well to remember to estimate the patient's weight at what it should be.

I find it easier to work with one variable factor in these cases, namely, insulin. There is no point in obtaining urinary sugar freedom on a small diet and a certain dose of insulin only to unstabilize the patient by raising the diet and increasing the

TABLE III.

Tabular Record of F.G., a Female, aged Thirty-eight Years, who had Glycosuria in the last Four Weeks of Pregnancy and for Eight Weeks after Childbirth.

Date.	Results of Glucose Tolerance Test, showing Percentage of Blood Sugar.				
	Fasting.	Half an Hour after Glucose.	One Hour after Glucose.	One and a Half Hours after Glucose.	Two Hours after Glucose.
November 5, 1937	0·09	0·16	0·19	0·15	0·15
June 1, 1938	0·10	0·16	0·18	0·12	0·10

insulin. Give what is thought to be the final diet at the beginning of treatment and vary the insulin alone until sugar freedom occurs.

In recent years our ideas on the amount of carbohydrate which should be allowed in a diabetic diet have been modified considerably. Whereas a few years ago it was the practice to provide only the minimum amount of carbohydrate compatible with freedom from ketosis, it is now usual to allow much more carbohydrate and to reduce the fats proportionately. It is a matter of experience that insulin requirements of patients taking low carbohydrate diets are considerably higher than in those to whom high carbohydrate feeding is given. This paradoxical observation is probably due to the stimulation of production of insulin by reasonable quantities of carbohydrate. At the present time, in the majority of cases, I am in the habit of using diets whose values vary as follows: carbohydrate, between 125 and 200 grammes; protein, 70 to 90 grammes; and fat, 80 to 100 grammes a day. The effect of these higher carbohydrate diets is often striking. The patients have a feeling of well-being which is frequently absent on diets high in fat; also a greater ease of living and a more liberal variation of meals are possible.

Another type of patient, middle-aged and obese, is handled on different lines. He is frequently difficult to manage; he may not feel ill, and is rather inclined to resent interference with his accepted modes of life, complaining that he does not feel any better when his urine is sugar free. Danger, in such a case, does not lie within the first few weeks or months of his seeking medical advice. This is the type of patient who, if treated in a cavalier fashion by being told that "a little bit of sugar in the urine does not matter", returns in five or ten years' time, blind from retinitis or maimed by diabetic gangrene. It is my opinion that this group of patients demands just as much attention as does the acute adolescent type. Far from increasing the weight of such a patient by a large diet it is frequently necessary to reduce the weight considerably. The process of obtaining urinary sugar freedom may be accomplished by semi-starvation on a relatively small diet for a short period, this being followed by deliberate underfeeding until the weight approximates to normal. After this the diet can be increased so that the weight will remain at a stationary level. Many of these patients will not need insulin, and even if it is necessary in the early stages of treatment, it may often be discontinued with the improvement in carbohydrate tolerance accompanying the loss of excessive weight.

Protamine Zinc Insulin.

The insulin of everyday practice is administered by subcutaneous injection, usually 15 to 30 minutes before a meal, and, according to the severity of the case, is given once or twice and, rarely, three times a day. It has an approximate pH of 3·5 and its absorption time is rapid, being maximal in anything from three to six hours. For some years the idea of prolonging the action of insulin and of delaying its absorption has attracted attention from experimental workers, and after various attempts had been made to achieve these objects the first commercial preparation of value resulted from the work of Hagedorn. He found that by combining insulin with a monoprotamine he obtained an insoluble compound which, when adjusted to approximately the pH of the tissue fluid, liberated insulin at a much slower rate; the use of protamine insulin prevented any violent fluctuation of the blood sugar, and so hypoglycæmic symptoms were less frequent and less severe. In many instances the use of protamine insulin was responsible for a reduction in the total daily dose and often it was possible to control the diabetic state by one injection per day. Scott found that, by the addition of small quantities of zinc to protamine insulin, its action was even more prolonged and that protamine zinc insulin was much more stable chemically than protamine insulin. Within the past two years there have appeared numerous articles by workers who have hailed enthusiastically the advent of these insulin compounds as marking a new era in the treatment of diabetes. The use of a slowly absorbed insulin possesses many advantages both from the patient's point of view on the grounds of convenience and from that of the physician on the grounds of more even and prolonged action. Up to the present time my experience of these new compounds has been limited to protamine zinc insulin. My findings have been published in detail elsewhere, but are, as yet, too inconclusive to permit of any dogmatic statement. I am convinced that it has a definite value in the treatment of diabetes; but I consider that the technique of using it is entirely different from that employed in the use of regular insulin. If one is to give all the extraneous insulin required by a patient only once each twenty-four hours, it seems that much more attention must be paid to the distribution and the type of carbohydrate food taken at each meal. I have been able to stabilize satisfactorily many patients by the use of protamine zinc insulin; some of these had been taking doses of regular insulin and others had been previously untreated. However, in some instances I have experienced extraordinary difficulty because the patient's response to this insulin appears to vary greatly from day to day, and I have been unable to maintain them in a satisfactory state of stability without the additional use of regular insulin. In two cases in a series of thirty-four I have been forced to return to the previous control with regular insulin alone.

Diabetes in Children.

In no aspect of the treatment of this disease has there been a more striking change following the introduction of insulin than in the control of the diabetic child. Although not common, diabetes in children is, as a rule, severe, and before the dis-

covery of insulin the mortality rate from diabetes in children was nearly 100%. White's figures for 519 children between 1922 and 1931 give a percentage of 93 living at the end of ten years. My own figures, based upon a group of 62 children observed during the past ten years, approximate to this with a 90% survival rate.

There are certain features of treatment which are peculiar to the diabetic child. Firstly, its energy requirements demand a higher Calorie intake weight for weight than is needed by an adult. Astonishment is sometimes expressed at the amount of food which a diabetic child will eat; but it is my experience that such a child should always be well fed. If it is not, it will obtain food, and in my opinion it is better for it to be given an adequate diet under supervision than for it to take food surreptitiously because of hunger. Higher carbohydrate diets have proved of very great value, as they permit of an almost normal diet, which is important because, in many instances, if the child is deprived of too many of the things which other children eat, it may develop feelings of difference from its fellow beings, and all sorts of behaviour problems ensue. Secondly, the education of the child is largely a function of the mother, and I would go so far as to say that the prognosis for the child is considerably influenced by the intelligence and cooperation of the parent. The careful training of the mother is probably the most important single feature in the control of the juvenile diabetic, and with appropriate treatment the child will live and grow in a fashion which is little removed from normal. Six patients in my series of 62 have died—one from influenzal pneumonia, one from pulmonary tuberculosis and four from lack of parental cooperation. The variable activities of the child, together with its relatively small capacity for glycogen storage, when compared with the adult, sometimes make stabilization a matter of difficulty, and on occasions it is almost impossible to keep the urine constantly sugar free and at the same time to avoid the symptoms of insulin overdosage.

Intercurrent Illness.

When a diabetic patient becomes ill from any cause, his usual routine is apt to be disturbed. If the illness is such that it involves no gastro-intestinal disturbance, the patient can continue with his usual diet; but it must be remembered that inertia, such as rest in bed, or infection is apt to demand an increase in insulin dosage. Those patients who usually do not require insulin may have to take it until the illness is past. On the other hand, if gastro-intestinal disturbance is present, and the patient is no longer able to eat the ordinary diet, a situation arises which demands constant attention. It is a common experience that in these circumstances the patient, unable to eat his usual food, will often omit his dose of insulin. He commences to draw upon his body tissues for energy purposes and, lacking available or usable carbohydrate, will develop a ketosis which may rapidly progress to diabetic coma. At such a time the main object of treatment is to avoid or control the ketosis, and the maintenance of a constantly sugar-free urine becomes of secondary importance. It is not humane to expect a patient who is seriously ill to be restricted to any one formula of diet. A sick person requires indulgence and so does a sick diabetic. Easily assimilated carbohydrate food in a fluid form should be given, combined with a fluctuating scheme of insulin dosage which is governed by the urinary findings. The urine must be fully examined at frequent intervals throughout the day. In grave illness, when it is impossible for the patient to take food by mouth, there must be no hesitation in commencing continuous intravenous infusion of 10% glucose in saline solution and in giving insulin in adequate amounts. I would again emphasize the fact that in the presence of infection and fever insulin is often less effective than in normal circumstances and the insulin dosage has to be temporarily increased.

TABLE IV.

Chart of Insulin Dosage During Intercurrent Illness.

Result of Benedict's Test.	Dosage of Insulin (Units).		
	Before Breakfast.	Before Lunch.	Before Dinner.
Blue	10	7	10
Green	12	10	12
Yellow	15	12	15
Brown	18	16	18
Red	20	18	20

Ketosis and Coma.

Failure to recognize the principles just enunciated may cause a degree of ketosis resulting in coma and death.

In the presence of severe ketosis there is no time to be lost, as every hour may influence materially the patient's chances of recovery. Ketosis is progressive and, if not arrested, will prove fatal in the majority of cases. Coma is preventible and, since the introduction of insulin, has ceased to be the dreaded complication of former years.

The principles of treatment are simple, and are concerned with the relief of ketosis and with the prevention of the circulatory depression which accompanies the later stages of this condition. Insulin is given frequently and in large doses, together with an adequacy of easily absorbed carbohydrate, until it is apparent from decrease in the degree of air hunger and of the amount of ketone bodies in the urine, that the state of acidosis is lessening. It is an accepted clinical fact that the state of ketosis is associated with antagonism to insulin, so that some hundreds of units of insulin may be required within a few hours. A constant watch must be kept upon the state of the circulation, a falling blood pressure and a rising pulse rate being signs of impending danger and demand-

ing the immediate use of hypertonic (1·8%) saline solution intravenously and the application of cardio-vascular stimulants. Death in coma is usually due to one of three causes: circulatory failure, renal failure or inadequate insulin dosage. Proper recognition of this fact is essential if treatment is to be successful.

Surgery and Diabetes.

Whereas formerly surgery was undertaken only as a life-saving measure, diabetic patients of today undergo the major procedures of surgery in comparative safety. During the period 1929 to 1936, 143 major operations were performed upon diabetic patients in the Alfred Hospital. There were 27 deaths, a mortality rate over all of 19%. The details of this series are shown in Table V. Notice is drawn to the fact that gangrene was responsible for almost one-half of the fatal cases.

The sufferer from diabetic gangrene is not a favourable subject for any surgical procedure; he is usually the victim of neglected or undiagnosed diabetes, he is arteriscleroticc, he may have some degree of peripheral neuritis, he is suffering from toxæmia because of absorption of the products of tissue decay, and he is often hampered by hyperglycæmia. Gangrene, apart from that following serious trauma, is a disease of the middle-aged and elderly patient, and may result from almost negligible injury, such as the pressure of an ill-fitting shoe or darned sock, the paring of a corn, or the cutting of an ingrowing toenail. So insidious may be the arteriosclerosis, so mild the diabetes, that it is not unknown for gangrene to be the initial reason for seeking medical advice; and by the time gangrene has developed the arterial system is already seriously involved. The leg suffers far more than the arm, for obvious reasons: the influence of gravity and the poorness of its collateral circulation. I have often observed the extreme degree of arterial blockage which is present in limbs removed because of diabetic gangrene, and it is of fundamental importance to recognize that this arterial damage is found more often in the larger arteries of the leg than in the arterioles of the foot. The occurrence of trauma or infection in such a limb demands an increased vascular supply, which is not forthcoming. I have been impressed by the general lack of appreciation of this fact in the management of gangrene. A poor blood supply and a high blood sugar content, together with neuritic changes of a trophic or anæsthetic type and the known vaso-constrictor effect of damaged tissues, present ideal conditions for bacterial growth. Yet to these there is often added a foment which may burn the affected area, without the slightest hope of improving the blood supply, the only effect being to provide even more favourable conditions for the spread of infection.

The only measures which make for success in the management of gangrene are those designed to improve the circulation of the whole limb, to control the diabetic state, to maintain a dry gangrene in a dry state by non-irritant dressings, and in the case of moist gangrene to prevent the spread of infection by early incision and drainage.

Infection in some form was responsible for almost one-quarter of the remaining deaths, a striking example of its seriousness in diabetes. It is to be feared because it initiates a vicious circle; insulin becomes less effective, the blood sugar content rises and more favourable conditions result for bacterial spread. Usually the indication is for early radical treatment of infection, as the diabetic state is more easily controlled when adequate drainage is provided.

What are the dangers likely to be encountered in diabetic surgery? The routine testing of urine for sugar is a necessary preliminary to any operation, as surgical procedure in an undiagnosed case is fraught with peril. With a known diabetic there is no rule-of-thumb procedure of insulin dosage or diet which can be applied in every case, and close cooperation between physician and surgeon is essential. If infection is present, if operation is a matter of urgency, if the patient's condition will suffer from the delay of surgical intervention, it is wise to operate first and treat the patient for diabetes later. If time permits, the object of preoperative treatment is to anticipate the possibility

TABLE V.

Operations Performed on Diabetic Patients at the Alfred Hospital during the Years 1929 to 1936.

Year.	Total Operations.	Deaths.	Amputation.	Incision and Drainage.	Mastoidectomy.	Removal of Cataract.	Gynæcological Operations.	Sympathectomy.	Amputation of Breast for Carcinoma.	Prostatectomy.	Appendicectomy.	Operation on the Gall-bladder.	Operation on the Thyroid.	Cure of Hernia.	Operations on Antra and Tonsils.	Laparotomy.
1929–1930 ..	11	6	6 (5)	2 (1)	1	1	1									
1930–1931 ..	17	2	5 (1)	5 (1)	1	3	2	1								
1931–1932 ..	30	4	4	10 (2)		7 (2)				2	2	2		1	2	
1932–1933 ..	25	4	0	9 (2)		3	3		1		2 (1)	1 (1)	1			2
1933–1934 ..	22	5	6 (4)	5		2	1					1	1 (1)			1
1934–1935 ..	18	4	7 (3)	4		1						2 (1)				
1935–1936 ..	20	2	1	5		2	2 (1)				2	3 (1)	2		2	1
	143	27	29 (13)	40 (6)	2	19 (2)	9 (1)	1	1	2	11 (1)	9 (3)	4 (1)	1	11	4

(NOTE.—The figures in parentheses represent the numbers of deaths.)

of post-anæsthetic ketosis by liberal feeding with carbohydrate and adequate doses of insulin. These factors, together with the selection of the most appropriate anæsthetic, make for success in diabetic surgery. The post-operative management for a few days should be concerned with the control of ketosis, although a continuous state of sugar freedom is desirable fairly soon after operation in order to facilitate the proper healing of tissues.

Other Features.

Two other points demand attention, the first being concerned with diagnosis. The occurrence of ketosis is at times associated with a constant deep-seated pain, which may be felt anywhere in the abdomen or thorax. The so-called "diabetic abdomen" is at times difficult to diagnose from acute appendicitis, acute cholecystitis or other abdominal emergencies. If time permits, the effect of treatment of the ketosis should be watched for some hours, but if doubt then exists it is wise to operate. The other point is concerned with the fallacy of urine testing as a guide to the state of diabetic control. In the diabetic of long standing the renal threshold to glucose may be raised very considerably, in which case a urine free from sugar may be deceptive. I have known a patient whose blood sugar content was 0·31% and whose urine contained no sugar at the time. Failure to recognize this possibility contributed largely to the loss of an eye following an operation for cataract.

The Necessity for Proper Control.

The question of control of the diabetic state having been dealt with and its importance having been stressed, the questions may be asked: Why be so strict? What does it matter if a patient has a little sugar in his urine; he feels none the worse for it and he feels none the better when it is absent; provided he is kept out of the danger of coma, why do more?

In a recent publication Joslin has shown the causes of death in over 3,500 cases. From this it is seen that arteriosclerotic disease is increasing rapidly and is now the major cause of death in diabetes. The problem of arteriosclerosis in diabetes is yet another unsolved mystery, having certain peculiar characteristics in that its main incidence appears to be in the arteries rather than arterioles and capillaries. It is associated not so much with hypertension and consequent apoplexy and renal degeneration as with coronary sclerosis and gangrene.

Degeneration of the retinal vessels, the coronary arteries and the vessels of the leg are the penalties which follow the prolongation of life in the diabetic of today. It is a striking commentary upon our present methods of treatment that arteriosclerotic changes can be observed in quite an advanced state in the vessels of adolescent patients. While we are in complete ignorance of its causation, there is, in my opinion, not the slightest doubt that it occurs more frequently, more severely and earlier in those persons who from ignorance or neglect have failed to maintain proper control of the disease. Whether arteriosclerosis be caused by hyperglycæmia, hypercholesterolæmia or some other unknown factor, the middle-aged patient who does not manage his diabetes properly is likely to spend his declining years maimed or blinded. When it is recognized that by far the great majority of patients develop *diabetes mellitus* after the age of forty-five years the force of these remarks becomes apparent. When this arterial degeneration produces clinical evidence of its presence it is too late to expect any form of treatment to repair the ravages of neglect and to restore vision to an eye or integrity to a limb.

In conclusion, I would suggest that, although much has been achieved in improving the outlook for sufferers from *diabetes mellitus*, we should not be satisfied with the mere prolongation of life; we must also endeavour to prevent complications by the proper use of our present knowledge and by encouraging the cooperation of our patients.

THE TREATMENT OF AMBULATORY DIABETICS WITH ZINC PROTAMINE INSULIN.

By KEMPSON MADDOX AND MADELEINE SCOTT.

(From the Diabetic Clinic, Royal Prince Alfred Hospital, and the Department of Medicine, University of Sydney.)

THE imitation of the natural delicate control of insulin concentration of the blood by diurnal injections of ordinary soluble or standard insulin is a crude one. Actually, its undoubted success in the reduction or abolition of glycosuria seems, on first consideration, remarkable. The conversion of a glycosuric individual, with diabetic symptoms, to apparent normality, by the injection of five to ten units twice a day, is a fairly common experience. It reveals an extraordinary fineness of control when the net result of carbohydrate metabolism can be varied by such a seemingly insignificant insulin supplement. The knife edge of sugar balance is, according to Lawrence's theory. maintained by a continuous secretion of pancreatic insulin, which is suddenly increased manyfold according to the post-prandial concentration of blood sugar.

It has been the aim of many experimenters to reproduce this steady state of insulin secretion, to which the pancreas returns an hour or so after meals and during periods of digestive repose, such as the hours of sleep. Insulin has been combined with various oils, precipitants of protein, with adrenaline and other vasoconstrictors, in an attempt to prolong its time of absorption. To Hagedorn, of Copenhagen, belongs the credit of discovering that a monoprotamine, an amino-acid from fish sperm, could absorb insulin and retain it at the site of injection for twelve to twenty-four hours, releasing it sufficiently slowly to create a fair imitation of the natural endogenous pancreatic

process. The protamine and insulin were mixed with a phosphate buffer, in order to bring the mixture to the pH of the blood. After an extended trial of over two years at the Insulin Hospital, Copenhagen, where the prolonged effects of the substance were thoroughly confirmed, protamine insulin was marketed generally. It was still found necessary to administer the insulin twice a day, and frequent adjustments, dietetic and otherwise, were necessary; but Hagedorn proved conclusively that the average blood sugar level over twenty-four hours was infinitely improved in patients previously treated with ordinary or standard insulin. The wide post-prandial excursions of blood sugar level were smoothed out to a most satisfactory degree. Shortly after this new insulin became available, Scott and Fisher, working in the Connaught Laboratories, Toronto, found that the addition of several substances, of which zinc, bismuth and calcium were the chief, further prolonged the action of regular insulin and of protamine insulin. The effects of a single injection of this triple compound were found to last as long as seventy-two hours. The zinc combination was generally adopted in June, 1936, and the turbid compound, with the zinc in chemical combination with the insulin, is now generally available in strengths double and quadruple that of standard insulin (40 and 80 units per cubic centimetre). Zinc in the amounts used for this purpose (1·0 milligramme to 500 units) has not been found to produce any signs of metallic intoxication, and it is quite free from any local irritant effect. It has the further effect of stabilizing the mixture so that no mixing with an alkaline buffer is necessary before use, though thorough shaking is essential. The choice of zinc was not fortuitous, as large amounts exist in the human pancreas, liver and bone, and it was found that even protamine insulin, when completely deprived of all traces of zinc, had no more prolonged action than regular insulin hydrochloride. Crystalline insulin also contains appreciable amounts of zinc; but, according to Altshuler and Leiser, this does not account for its prolonged action.

We tested the stability and potency of the first batch received from America early in 1937, and found a prolonged depreciation in the blood sugar content of normal and diabetic individuals, similar to that claimed by the manufacturers. Any further properties had been fully described already and no further experimental inquiry suggested itself.

The first British reports on the value of and indications for zinc protamine suspension were published by R. D. Lawrence and Nora Archer in March, 1937. Valuable principles of treatment were laid down to which reference will be made later. These authors treated 42 patients with diabetes of all grades of severity by one injection a day of zinc protamine insulin suspension, alone or in combination with ordinary insulin. They considered that careful study of each case was essential and close observation necessary. They drew attention to the frequent variability in the effect of the new insulin from day to day, ascribing this to a varying rate of absorption. H. P. Himsworth simultaneously discussed the new insulins, and found a place still left for protamine insulin alone, or in combination with the zinc protamine insulin compound. This is one of the most thoughtful and broadminded articles we have read. A series of most instructive articles by Rabinowitch, Fowler and Corcoran, of Montreal, covered almost all the groundwork necessary for the full exploitation of this remedy. They formed a high opinion of its usefulness, especially in the former "insulin waster", and recorded only eight failures in 132 selected patients; only three of the 132 patients required more than one injection a day. Since then reports of the use and value of the new insulin compound have poured into medical literature, especially from America, so that Joslin has recently made the surprising statement that no less than 1,250 of his patients have come to depend on protamine zinc insulin since the inauguration of what he terms the "Hagedorn era". Of these individuals, 53% take protamine zinc insulin alone and 47% in combination with regular insulin. Only 30 of these 1,250 patients have had to return finally to regular insulin. He estimated that there were 70,000 more diabetic patients taking insulin in the United States of America in 1937 than in 1936, as a direct result of the benefits of protamine zinc insulin. The degree of control secured in Joslin's series of 1,250 patients was as follows: excellent in 10·2%; good in 60%; fair in 27%; poor in 2·7%. As compared with 64% of patients well controlled by protamine insulin, 73% are well or excellently controlled with zinc protamine insulin. Smith and Grishaw, a year ago, reported their results in the treatment of 150 patients, of whom 79 had severe diabetes, observed over one year. In a well-balanced summing up they state that over 56% of insulin-sensitive diabetics have been able to continue on one daily dose as compared with 29% among the insulin-resistant patients. Mosenthal has recently defined more distinctly than any other author hitherto, the types of diabetics who are better treated with regular insulin than protamine insulin, and it is apparent that the natural enthusiasm of the majority of earlier workers must undergo the inevitable limitation. Campbell, of Toronto, using protamine obtained from the Canadian king salmon, was able to obtain a longer hypoglycæmic effect than Hagedorn. He also reports his experiences (which included no difficulties) with the protamine zinc compound in the treatment of elderly diabetics. His diet was of the older type, rich in fat. The patients effected a considerable saving in the units of insulin required, and hypoglycæmic reactions were rare. On this account he advocates a return to a lower carbohydrate diet if hypoglycæmic difficulties occur. His generalizations on a small series are, however, too sweeping. E. J. Kepler sums up the experience at the Mayo Clinic up to the end of 1937 as follows:

Protamine zinc insulin has facilitated treatment in many cases of diabetes, especially those in which the disease was of moderate severity. Earlier and severe cases are still a problem in treatment.

Lawrence, in a personal communication, writes: "Difficult cases are still difficult."

A hundred further opinions could be quoted; but it is apparent that authoritative opinion in English-speaking countries is favourably impressed by the new insulin. Some recent reports even suggest the view that it is a "cure-all" for diabetics. So far only sporadic case reports have appeared in this country.

We felt that it would be better to watch carefully a few dozen individuals taking protamine zinc insulin for some months rather than quickly to attempt to collect a large enough series to be of true statistical value. Communication with a large Melbourne clinic proved that a similar plan had been adopted there, and it was agreed to pool the information so obtained. Thus Downie has reported his experiences of a group of 32 patients who have largely been treated in hospital, but have not been confined to bed. This is the ideal arrangement, and admission to hospital has been insisted upon by most investigators and therapists.

The series forming the material for this report also consists of 32 patients, mostly diabetic workers who cannot afford the time to enter hospital. We have never had the occasion to regret ambulatory treatment with ordinary insulin. No adjustments to increased exercise or changes in timetable are necessary in the case of the diabetic out-patient. It would seriously limit the distribution of the benefits of protamine zinc insulin if the precaution of admission to hospital was unswervingly insisted upon. There are enough variables without a sudden change from hospital to home life. Treatment of the ambulatory diabetic with protamine zinc insulin has been advocated also by Mosenthal, who states:

The most permanent satisfactory regimen, the quickest regulation and the greatest economy of time and expense are accomplished by office or dispensary management as compared to hospitalization.

It may take slightly longer to stabilize the carbohydrate metabolism outside hospital; but as changes in the dose of protamine zinc insulin compound should not be made more frequently than once in five days, the time and expense of indoor treatment may become a still further deterrent to the acceptance of its benefits. Again, the "danger" period, or rather the time when severe nocturnal hypoglycæmia is most frequently encountered, is late in treatment, usually after discharge from hospital, when unanticipated worries and exercise, irregular meals *et cetera*, disturb the usual routine. Week-end treatment in hospital after apparently satisfactory outdoor stabilization for the purpose of obtaining a twenty-four-hour blood sugar curve would be an excellent manœuvre from all points of view, except perhaps that of the biochemist.

Rosenthal and Finkelstein report satisfactory results from the treatment of 70 ambulant patients with protamine zinc insulin under conditions strikingly akin to our own. There can be no doubt, however, that observation of a twenty-four-hour blood sugar curve is an immense advantage; but control can be considered satisfactory if (*a*) the patient's urine is sugar free throughout the day, (*b*) the patient's fasting blood sugar content is between 80 and 120 milligrammes per 100 cubic centimetres, (*c*) the blood sugar value is below 160 milligrammes per 100 cubic centimetres in the mid-forenoon, and (*d*) there are no evidences of hypoglycæmia in the late afternoon or evening. We have depended upon the results of five urine tests with Benedict's solution per day by patients partly selected for their reliability, satisfactory standard of intelligence, and education in the diabetic life. Estimations of the fasting blood sugar content have been made at varied intervals, not more frequently than once a month. The patients have attended not more than once a week, when their weight and other physical characters have been checked, tests for sugar and acetone have been performed on a specimen of urine passed at the clinic, and a review of the week's urinary chart and experiences has been undertaken. A typical chart is shown (Table I). It will be observed that considerable emphasis is placed upon the necessity of obtaining and testing what might be called the "shaving" specimen, that is, urine secreted in the period between emptying the bladder of night urine and taking breakfast. This is, of course, a direct reflex of the fasting blood sugar.

TABLE I.

Urine Chart for Patients taking Zinc Protamine Insulin (Diabetic Clinic, Royal Prince Alfred Hospital), showing Variability in Control often encountered when Moderately Large Doses of Zinc Protamine Compound are taken.

Name: E.H. *Insulin Dose:* Morning: Zinc Protamine Insulin, 45 units.

Week ending April 30, 1938. Evening: ——

Day.	On Rising.	Just Before Breakfast.	10 to 11 a.m.	4 to 5 p.m.	8 to 9 p.m.
Monday ..	Blue.	Blue.	Blue.	Blue.	Blue.
Tuesday ..	Blue.	Blue.	Blue.	Blue.	Blue.
Wednesday ..	Green.	Blue.	Green.	Green.	Brown.
Thursday ..	Blue.	Blue.	Green.	Green.	Green.
Friday ..	Blue.	Blue.	Blue.	Blue.	Blue. Reaction 4 a.m.
Saturday ..	Red.	Green.	Green.	Blue.	Blue.
Sunday ..	Blue.	Blue.	Green.	Red.	Green.

(*N.B.*—(i) If away from home at these times, change the day about so as to cover all the times specified by the end of the week, or arrange to take a specimen home and test it there later; on Sunday test at all the above times. (ii) If you have an insulin reaction, indicate it at the appropriate time on the chart.)

Insulin Dosage and Treatment of Patients Already in Receipt of Standard Insulin.

The patients chosen were: (*a*) those who were behaving unsatisfactorily on standard insulin, including some "insulin wasters"; (*b*) those who had time to test their urine five times a day; (*c*) those who were particularly anxious to reduce the number of insulin injections per day; (*d*) children. The number of patients already in receipt of standard insulin was 21.

The administration of the compound insulin half an hour before breakfast was the recognized routine at the time of arrival of our first samples. Our earliest patients were asked to follow the scheme outlined by Lawrence and Archer, namely, to give themselves three-quarters of the former total daily number of units in protamine zinc insulin before breakfast, and to add thereto half the usual morning dose of regular insulin, omitting insulin at night altogether. This was attempted in eight of our cases. These patients were asked to test the urine by Benedict's test on rising, an hour after rising, at 10 or 11 a.m., at 3 or 4 p.m., and at 8 or 9 p.m. At first the two types of insulin were mixed in the same syringe; but later we formed the definite impression, unfortunately not proven in the laboratory, that better control followed injection by separate syringes into different areas of subcutaneous tissue. The immediate effect on those patients who had been under satisfactory control, was a return of glycosuria, either complete or at irregular intervals, usually in the morning, early or late. This has been universally recognized, and is due to the long latent period before the cumulative action of the zinc protamine insulin has its final influence. For this reason it is unwise to make any fresh adjustments to the dose before at least three or four days have elapsed, since Lawrence has demonstrated that there is a 72-hour effect after administration of zinc protamine insulin. Actually our patients were not seen for a whole week, and were not at this stage permitted to alter their own dosage, unless severe hypoglycæmic reactions were experienced. The patients were invited, in such an event, to report to the sister in charge of the clinic, who was empowered to make any provisional minor alterations that she deemed advisable in insulin or diet arrangement.

After a few months' observation of patients on this régime, we have concluded that three-quarters of the previous total insulin intake as zinc protamine insulin was often an insufficient, though certainly a safe, basis for commencement. It has been our experience that after a diabetic relapse, even when apparently unassociated with infection or psychological instability, reattainment of control has meant at least a 25% increase over the original insulin dosage, for a time at least. Frequently a permanently higher insulin intake is required. A sudden change to zinc protamine insulin, after a period of satisfactory control by regular insulin, constantly reproduces this phenomenon. The new insulin has not only to supplant the effects of the old, but has in addition to overcome the temporary further deterioration of carbohydrate tolerance which, as is well known, follows a period of hyperglycæmia. Severity of hypoglycæmic reactions at a later stage as tolerance gradually improves may well be associated with the large size of the dose necessary to combat this double difficulty. An increase or decrease in dosage by five units at a time is a reasonable and safe margin for patients taking regular insulin, at least for those taking more than 30 units a day. It has been our experience, however, that a smaller increment, usually three units, of protamine zinc insulin is sufficient for those individuals taking a total of 30 units a day or less. In the higher dose class (30 to 50 units a day) changes of five units at a time are tolerated satisfactorily, while in the cases in which the patients receive 50 or more units a day, time can often be saved by steps of ten units each week.

A great deal of allowance must be made for individual variability in response to the new insulin. Spontaneous differences in effect on a constant insulin and diet consumption are the order of the day. Some and perhaps all of these variations are explicable on grounds of (*a*) failure to shake the bottle of insulin and so distribute the protamine *plus* absorbed insulin evenly throughout the contents; (*b*) failure to clean the syringe properly of all vestiges of methylated spirit, which precipitates the compound in a more insoluble form; (*c*) variation in the absorptive capacities of different areas of subcutaneous tissues. This is a factor in all hypodermic therapy which has not yet been properly investigated. The effect of massage, either deliberate or as a result of casual friction or muscular exercise, is by no means insignificant. External and therefore skin temperature affects superficial vascularization to a degree as yet undetermined. Some of the severest hypoglycæmic reactions we have encountered have followed an unusual degree of muscular effort. Where this can be anticipated, patients are instructed to take some additional carbohydrate, for example, two biscuits or a lump of sugar, beforehand.

Of the seven patients who were given a dose of zinc protamine insulin of a lesser number of units than the total units of ordinary insulin on which they had been previously stabilized, five patients are satisfactorily controlled with a lower dosage of zinc protamine insulin in units as compared with their former total number of units of ordinary insulin. The two patients taking more insulin than before have milder diabetes, and the difference in insulin dosage required is only in the region of five units a day. When the total number of units of both types of insulin are compared in this first group, however, three patients are found to be taking less and four more than previously.

As regards the technique of reduction of injections to one per day, Lawrence and Archer's advice has been followed, namely, gradually to eliminate the night insulin by five units at a time, transferring some or all of it if necessary to the morning dose of ordinary insulin. Of the seven patients referred to above, only three failed to be controlled by morning insulin only. One of these patients is a pituitary dwarf of low mentality who forms a special problem, whose diet is completely uncontrolled, and who shows a ready tendency to hypoglycæmic convulsions. Two of the patients are

highly nervous subjects whose carbohydrate metabolism directly reflects their psychological instability. It would appear therefore that the method described above is usually successful and safe, tending to minimize the extent and duration of the hyperglycæmia inseparable from the transfer. The next plan to be followed was in accordance with more recent practice elsewhere. In a group of five patients zinc protamine insulin was employed in a dosage equivalent to the total regular insulin previously taken in twenty-four hours, in an attempt to reduce further the transition period and its accompanying glycosuria. Two of these patients required additional ordinary insulin in the morning of approximately one-third of the previous ordinary insulin intake to render their urine sugar free. The remaining three were stabilized on zinc protamine insulin alone, but in doses higher than those given at the commencement.

Four patients were tried on a higher dosage of zinc protamine insulin than was required formerly as a total daily intake of regular insulin. Actually this was an attempt to eliminate regular insulin altogether, and these patients were each transferred at once and entirely from regular insulin to zinc protamine compound. This proved a control within a week and virtually eliminated any tendency to transitional hyperglycæmia; but in each case hypoglycæmic attacks were experienced during the second and third weeks.

A further two patients were formerly in the habit of receiving one small daily dose of regular insulin at the hands of a visiting nurse. They always had pronounced glycosuria. Each was given a dose of zinc protamine insulin of one and a half times that previously administered as regular insulin. Subsequently the dose in one instance was increased by increments of ten units to five times this amount, after which the urine gradually cleared and hypoglycæmic reactions began. Satisfactory stabilization was reached at a figure three times the amount of the original amount of ordinary insulin. In the other instance twice the original amount of ordinary insulin was satisfactory.

Investigation of the time factor shows that the first group (initially receiving the smallest amount of zinc protamine insulin) required an average of four and a half weeks before satisfactory stabilization occurred. In the remaining groups stabilization was in many cases achieved within one or two weeks. No doubt if visits had been made to the clinic more frequently, say, twice a week, the month required to stabilize the first group could have been halved. Most patients said that they felt distinctly better on the new insulin than on the old, and they certainly appreciate the reduction in the number of injections required.

Treatment of New Patients and Those Not Already In Receipt of Standard Insulin.

The patients chosen for treatment *ab initio* by the new compound have had on the whole mild diabetes; but after a trial period on a suitable quantitative diet, it became apparent that they would require some insulin at least. Four were children, one was an adolescent and the remainder had passed the third decade. Lawrence and Archer suggest that such patients should commence with a trial dose of 30 units of zinc protamine compound before breakfast, with additional standard insulin if acetone is present. In general, we have used a smaller initial dose of fifteen to twenty units of the zinc compound, giving more or less afterwards as seemed indicated. Patients rendered aglycosuric by such initial quantities rarely require any supplementary doses of standard insulin. It is extremely difficult to predicate what the final amount will be, and stabilization of this type of patient takes longer than previously. The level of the fasting blood sugar before treatment is only an approximate guide to the real severity of the diabetic state and to the dosage of zinc insulin ultimately necessary. We have noticed several patients who appeared to have reached stability within a week or two of receiving their first dose of protamine zinc insulin, only to begin suddenly passing quantities of sugar again and ultimately needing two or three times the original amount of the compound. The total time taken in such instances for final stabilization has been as long as three months. Severe hypoglycæmic attacks have sometimes soon interrupted this latter stage of apparent success.

It has been our experience that a supplementary and simultaneous dose of ordinary insulin has been necessary for all patients finally requiring more than 40 units of insulin a day. To no "new" patients of this series has it been necessary to give additional insulin at night, although in the treatment of some "old" patients (those previously treated by soluble insulin), difficulty has been encountered in dispensing entirely with the nightly dose.

Shortly, the basal dose of the compound is adjusted until the "shaving" specimen (that passed one hour after emptying of the bladder on rising) of the following morning is devoid of sugar, the supplementary dose of insulin is adjusted until the "late morning" specimen is just sugar free. This may be called the "coarse adjustment". The "fine adjustment" is achieved by the transference of the carbohydrate of the food in small amounts from meal to meal.

Diet Arrangement.

All authors are agreed that a steady, even inflow of carbohydrate via the portal vein is the ideal condition to accompany the supposedly constant steady inflow of insulin from the site of the injection of zinc protamine insulin. This is a practical impossibility; but the patient, by religiously including morning tea, afternoon tea, and especially supper in his dietary, can actually have six meals a day in place of three. Owing to the latent period of action of protamine zinc insulin, it is usually desirable to give rather less carbohydrate for break-

fast than for lunch, and still less at lunch than at tea (or dinner). The importance of a reasonably substantial supper should be emphasized. Transference of small amounts (five to ten grammes) at a time of food rich in carbohydrate from one meal to another is the final process in complete adjustment, and the necessity for this varies with individual idiosyncrasies and habits. School children's sandwich lunch is always a difficulty. Usually they must eat some of this or an apple at the 11 a.m. playtime. We use the usual generous carbohydrate diets containing an average ration of 120 to 150 grammes of carbohydrate daily, and higher still for children. This type of diet seems to offer greater difficulties of control by zinc protamine insulin than by standard insulin. From comparison with the reports of others who have employed diets of lower carbohydrate value, the older type of diet rich in fat and poor in carbohydrate makes for readier stability, but is generally admitted to be physiologically less desirable.

Hypoglycæmia.

Hypoglycæmic attacks in patients taking zinc protamine insulin have been more frequently encountered than in those receiving regular insulin, especially in those patients who were ordered more than three-quarters of their previous total daily units as zinc protamine insulin. The attacks often occurred before the fasting blood sugar had been brought to its normal range, and as would be expected, were most common in the very early hours of the morning. The patients are often rendered difficult to arouse and, when awakened, are as a rule irritable and confused. A certain number of attacks were experienced in the late afternoon. Attacks occurring in the forenoon were usually found to be the result of too much supplementary ordinary insulin or to undue delay in taking the midday meal. The attacks were often severe and recovery was slow. In two patients nocturnal behaviour disorders were experienced.

In one patient hypoglycæmia may have possibly contributed to death. She was a sufferer from myocardial failure and on this account was confined to bed for two weeks before her death, which occurred suddenly during the night hours.

One patient experienced almost continuous headache and was found to have a blood sugar value varying from 50 to 90 milligrammes per 100 cubic centimetres. The headache disappeared after more satisfactory adjustment of her insulin dosage.

We found surprisingly low blood sugar values in the absence of any hypoglycæmic symptoms. Such patients would be readily precipitated into hypoglycæmia by any change in their usual régime involving additional muscular exercise.

The Use of Zinc Protamine Insulin in Special Conditions.

Coma.

We have no opportunity in an out-patient clinic to observe the effect of a particular mode of therapy in diabetic coma. My own experiences have been limited to three in-patients to whom an initial dose of zinc protamine insulin had been administered at the outset with the ordinary insulin, given in the same dose as one would use even in the absence of zinc protamine insulin, that is, 50 to 100 units. Each patient made an uneventful recovery in much the same time as might usually be expected. None of these patients, however, was dangerously ill. Records of the value of zinc protamine insulin in coma are becoming frequent.

Diabetes of Children.

The present series includes six children between the ages of ten and fifteen years. One of these required only 15 units of zinc protamine insulin a day in one injection. Another, of the same age, required 22 units; but two others, both older, each required 80 units of zinc protamine insulin a day *plus* in one case 25 units of ordinary insulin. Even then control is irregular; but no serious hypoglycæmic attacks have occurred. The diet of each of these children is in the 1,800 to 2,000 calories zone. Abundant reports, however, exist of the boon available in zinc protamine insulin for smoothing out the labile blood sugar curves of diabetic children.

Miscellaneous.

A patient died from pulmonary tuberculosis about two months after commencing treatment with zinc protamine insulin. Although febrile, he had been readily and satisfactorily stabilized. Zinc protamine insulin should be of considerable assistance in keeping the blood sugar steady in patients of this type. One of our patients with hæmochromatosis has presented no difficulties on changing over from regular insulin to zinc protamine insulin.

Results.

Our results have been arbitrarily classified as excellent, good, fair, poor, and failures.

I. Excellent.

Results have been regarded as excellent when home and clinic tests have shown the urine to be almost uniformly free from sugar, when such estimations of the fasting blood sugar content as have been made have resulted in figures approximating the normal range, and when hypoglycæmic attacks have been rare and mild, or entirely absent. (Four of thirty-two patients.)

CASE I (see Figure I).—I.S., a female, aged forty-eight years, formerly in receipt of a diet of 1,400 calories and 20 units of regular insulin twice a day, was glycosuric to a varying degree. Five months ago she was suddenly switched from the above régime to 30 units of zinc protamine insulin in the morning *plus* 15 units of regular insulin. Three days later she complained of a prolonged attack of hypoglycæmia, following which she stated she was giddy all the next day. The zinc protamine insulin was accordingly reduced by five units. She has remained on this dosage for four months without showing any hypoglycæmia and only very occasional glycosuria. Her fasting blood sugar content four months ago was 150 milligrammes per 100 cubic centimetres, and at time of writing 140 milligrammes per 100 cubic centimetres.

II. Good.

Results have been classified as good when home and clinic tests have been usually free from sugar, when fasting blood sugar estimations have sometimes given figures above the normal range, and hypoglycæmic attacks have been uncommon, but perhaps severe. (Fifteen of thirty-two patients.)

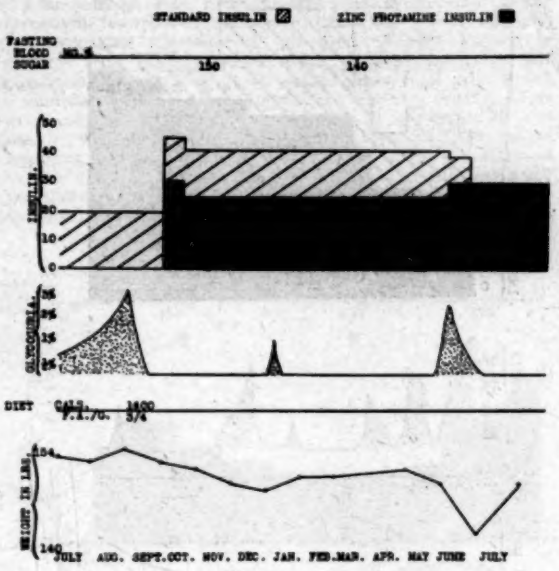

FIGURE I.

Graph showing satisfactory control in patient without necessity for continual increase in zinc protamine insulin, and permitting ultimately of elimination of the supplement of ordinary insulin. This patient is emphatic about her improved sense of well-being with the new insulin.

CASE II (see Figure IIA).—M.J., a female, aged forty-six years, four months before the time of writing, was taking the same diet as she had taken for four years. Her fasting blood sugar content was 186 milligrammes per 100 cubic centimetres, and she required 40 units of insulin a day in two equally divided doses. She was changed overnight to the zinc protamine insulin régime and asked to administer 50 units of zinc protamine insulin before breakfast each morning. The diet was rearranged into five equal meals. The immediate result of this was a hypoglycæmic attack thirty-six hours after the commencement of the new insulin treatment, and then sugar in fairly large amounts appeared in the urine at 10 a.m. and 5 p.m.; this, however, tended to clear by the early morning. A fortnight later the dose of zinc protamine insulin was increased to 60 units in the morning *plus* 10 units of ordinary insulin. The urinary response consisted of a trace of sugar at 5 p.m. and occasional hypoglycæmic attacks, which tended to be prolonged, at night. Her urine gradually became quite clear, and six weeks later she had gained 3·7 kilograms (six pounds) in weight. At this stage hypoglycæmia began to reappear about midnight, recurring an hour later in spite of the administration of sugar. Zinc protamine insulin was reduced to 50 units *plus* 10 units of standard insulin; but the attacks persisted, though they came somewhat less frequently. As a result the zinc protamine insulin was reduced to 40 units *plus* 10 units of standard insulin. She states that she feels very well. Her home tests reveal no glycosuria, even in the morning following a hypoglycæmic attack the night before, for which she had taken several lumps of sugar. She is very gratified with the fact of having to give herself an injection only once a day.

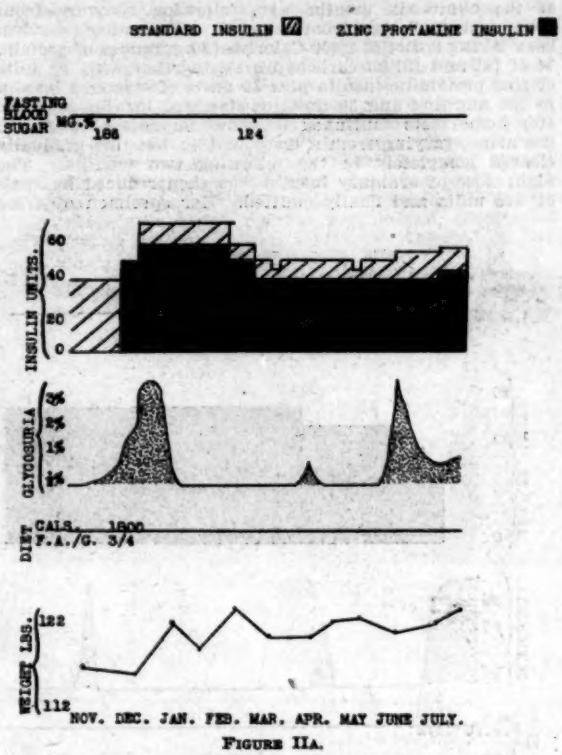

FIGURE IIA.

Graph showing satisfactory control by zinc protamine insulin.

CASE III (see Figure IIB).—W.W., a male, aged fifty-nine years, first came to the clinic with acute diabetes, having lost 18·9 kilograms (three stone) in weight, and with a fasting blood sugar content of 350 milligrammes per 100 cubic centimetres, together with ketonuria. He was immediately given a diet of 1,200 Calories, consisting of 52 grammes of protein, 58 grammes of fat and 115 grammes of carbohydrate. He was given 15 units of zinc protamine insulin compound a day. This reduced, but did not control, the glycosuria, so the dosage was raised by stages to 25 units, in one injection, in the morning. Three weeks after admission he had gained 3·2 kilograms (half a stone) in weight, and his fasting blood sugar content had fallen to 124 milligrammes per 100 cubic centimetres. He felt a definite improvement and has been able to return to his farm work. He insists that his present diet is adequate. He has now gained 9·5 kilograms (one and a half stone) in weight since he commenced treatment. He has had no evidence of hypoglycæmia beyond a little giddiness about noon on one occasion. He states that he tends to have a trace of sugar in the urine after a marked change in atmospheric temperature.

III. Fair.

Results have been regarded as fair when home tests *et cetera* have often shown sugar in the urine, when the fasting blood sugar content is frequently above the normal range, and hypoglycæmia has been sufficiently common to disturb the patient's comfort. (Six of thirty-two patients.)

CASE IV (see Figure III).—J.B., a female, aged twenty years, had suffered from three attacks of diabetic coma in nine years. Her bodily contour and the scantiness of axillary and pubic hair were such as to suggest some degree of hypopituitarism. She commenced attendance

at the clinic six months ago, following recovery from coma and discharge from hospital. Since then she has been taking a diet of 1,600 Calories (80 grammes of protein, 74 of fat and 151 of carbohydrate), together with 30 units of zinc protamine insulin *plus* 30 units of standard insulin in the morning and 30 units of standard insulin at night. Her home tests continued to show amounts of sugar in the urine, varying from a trace to 1%; but this gradually cleared completely in the following two months. The night dose of ordinary insulin was then reduced by steps of five units and finally omitted. Her specimen of urine

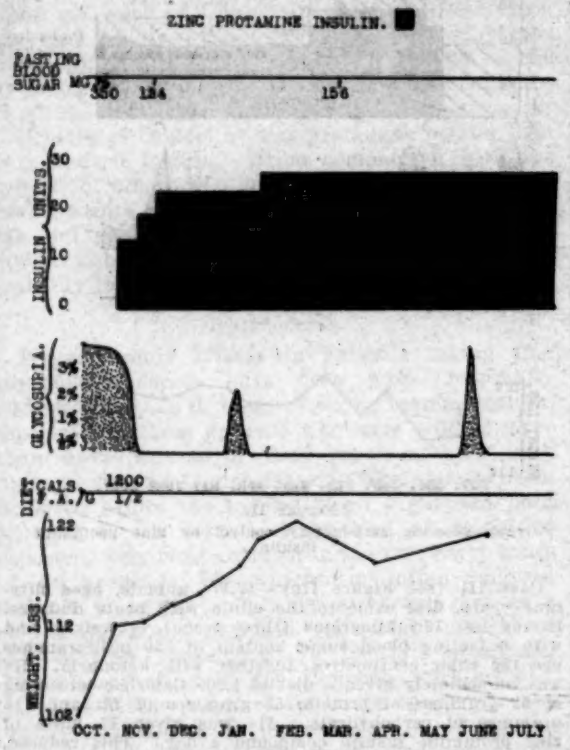

FIGURE IIa.

Graph showing "good" control of patient W.W. (a farmer doing strenuous work) by zinc protamine compound alone. No modification of dosage whatever has been required in seven months.

tested at the clinic continued to be sugar free, but the sites of injection of the insulin were stated to be painful. No signs of induration, however, were detectable. Abundant sugar reappeared in the specimen tested at 11 a.m., so the dose of zinc protamine insulin was raised to 80 units a day, together with 40 units of standard insulin, and as the sugar still persisted in copious amounts in the 5 p.m. and 11 p.m. specimens, the dose of zinc protamine insulin was raised to 100 units and the standard insulin to 50 units. But this increase failed to reduce the glycosuria at the times mentioned. The patient's own feelings were chiefly of tiredness and soreness of the arms. Her fasting blood sugar content at this period was 204 milligrammes per 100 cubic centimetres. Following advice to inject the zinc protamine insulin and standard insulin at separate sites, the glycosuria slowly disappeared, and for three months she was kept at an intake of 160 units. Occasional glycosuria appeared in the mid-morning. The fasting blood sugar content still varied between 204 and 260 milligrammes per 100 cubic centimetres. The dose of zinc protamine insulin at this stage was raised to 110 units and the dose of standard insulin to 65 units. Her mother now complained that she behaved very strangely and tended to be very drowsy all day, symptoms which disappeared after the reduction of the dose of standard insulin to 15 units in the morning. Some rearrangement of her carbohydrate intake is at present being undertaken.

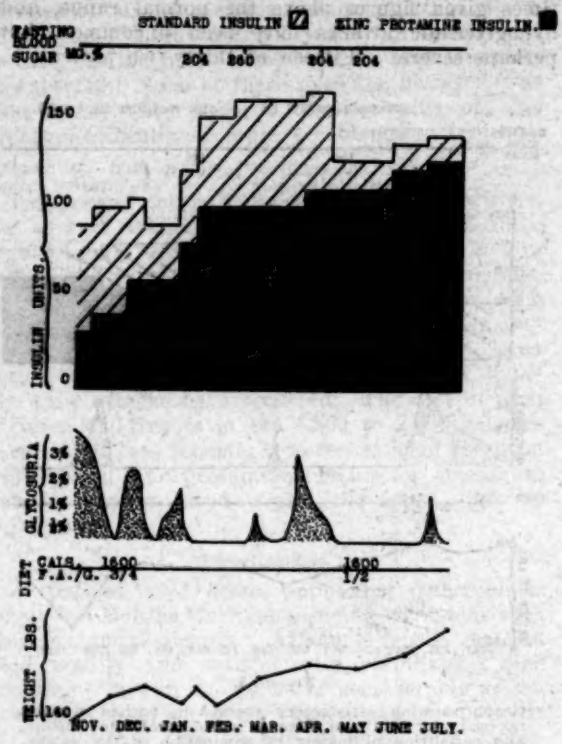

FIGURE III.

Graph showing ultimate control of diabetes in a young female, with progressive increase in weight, but only after progressive increases of zinc protamine insulin to a high figure. The change to a higher carbohydrate diet may have delayed stabilization.

IV. Poor.

Results have been regarded as poor when home tests have usually shown sugar present, when there is a high fasting blood sugar or when hypoglycæmic attacks are frequent. (Seven of thirty-two patients.)

CASE V (see Figure IV).—B.E., a female, aged nineteen years, had formerly taken a diet with a fuel value of 1,700 Calories, together with 40 units of regular insulin in the morning and 20 units at night. She entered hospital in pre-coma, during which period she was given zinc protamine insulin for the first time. The dose was increased from 30 to 70 units. Glycosuria still appeared in the late afternoon and evening. After her discharge she recommenced attendance at the clinic, on a diet of 1,400 Calories (60 grammes of protein, 68 of fat and 132 of carbohydrate), and taking 70 units of zinc protamine insulin before breakfast. Tests at home continued to show fairly heavy glycosuria in the late afternoon and evening; but her weight increased simultaneously. This increase in weight worried her for cosmetic reasons, and the diet at her request was reduced to a fuel value of 1,200 Calories, containing 52 grammes of protein, 67 of fat and 92 of carbohydrate. The dose of zinc protamine insulin was increased to 90 units at this stage. For a time her urine was completely sugar free and she insisted that her diet satisfied her. After six weeks, however, she began to experience hypoglycæmic attacks at 11 a.m., and

her insulin was reduced by steps to 60 units of zinc protamine compound in the morning. An estimation of the fasting blood sugar content, made at the point where she was taking 70 units of zinc protamine insulin a day, showed the rather alarming figure of 53 milligrammes per 100 cubic centimetres. Two months later her weight had fallen by 2·3 kilograms (five pounds), and the insulin intake had been reduced to 50 units of zinc protamine insulin, as fairly severe hypoglycæmic attacks had been experienced at the time of rising in the morning and at 4 p.m. This was not effective for long, and heavy glycosuria reappeared during the next six weeks in spite of progressive increase in the dose of zinc protamine insulin. Her fasting blood sugar content was now 132 milligrammes per 100 cubic centimetres, and she began to complain of neuritic symptoms. At the present time her intake of zinc protamine insulin is 120 units in one dose in the morning, and her home tests of urine show abundant sugar. Her weight has not fallen in spite of the low caloric value of the diet. Her neuritis has been symptomatically relieved by injections of vitamin *B* concentrate. Apparently she is just another "insulin waster".

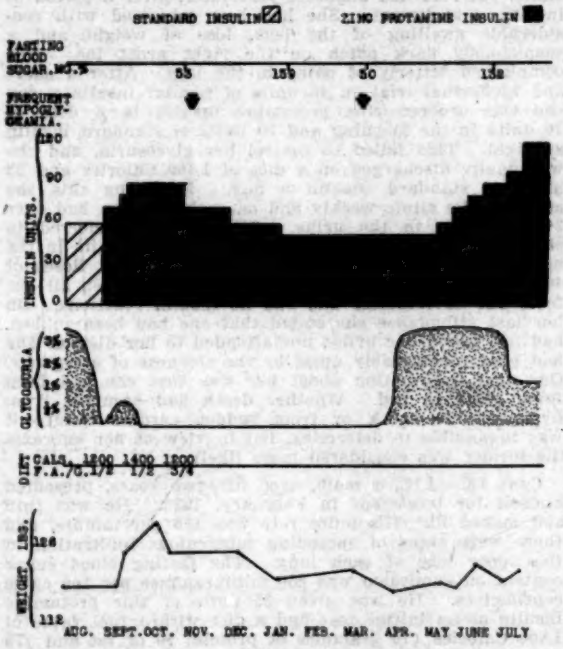

FIGURE IV.

Graph illustrating a good example of temporary control by zinc protamine insulin alone, followed by a sudden unaccountable breakdown or exacerbation, which has remained unchecked in spite of progressive increase to more than double the amount of zinc protamine insulin previously found effective.

V. Failures.

While every one of our patients is not consistently and permanently stabilized, we have had occasion to revert to ordinary insulin alone in the treatment of two patients only, admittedly sufferers from severe diabetes. The reason for the imperfect insulin action in these patients is obscure. They are certainly much better off with standard insulin before each meal.

CASE VI (see Figure V).—The patient is a female, aged twenty years, who attended the clinic for two years, having been admitted some ten months after the onset of her disorder. She showed considerable insulin resistance from the first, when the dose of standard insulin was increased to 100 units a day before her blood sugar value reached a normal zone. She formed one of a series treated by Hagedorn's protamine insulin, but unsuccessfully, in spite of various combinations with standard insulin. She was given 40 units of zinc protamine insulin in the morning and 20 units of standard insulin at night. Five days later prolonged hypoglycæmic coma occurred, which rendered the patient stupid and non-cooperative. It was only with difficulty that she was restored to her senses. Her fasting blood sugar decreased somewhat in the next ten days, but the urinary sugar continued to appear in the proportion of 3% for the next month, despite an intake of 90 units of zinc protamine insulin in the

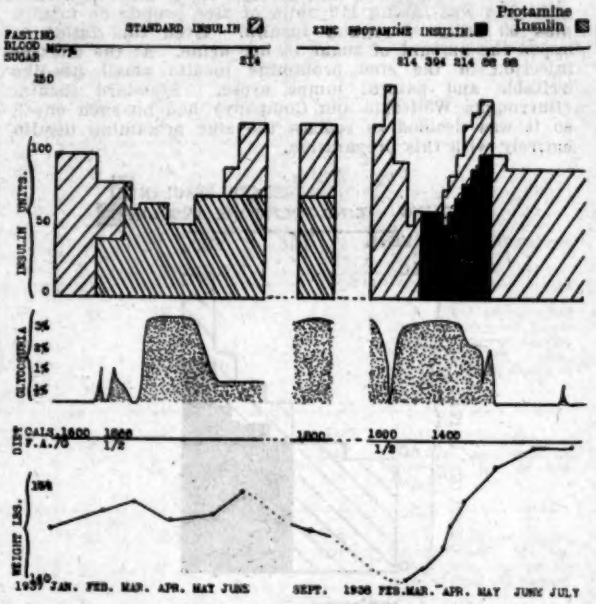

FIGURE V.

Progress of patient B.R. during eighteen months' fairly continuous observation. Illustrates superiority, in this instance, of standard insulin over (a) protamine insulin given during seven months of 1937, and (b) zinc protamine insulin given in three months of 1938.

morning and 40 units of standard insulin at night. At this stage occasional urine tests, either at 6 a.m. or 10 a.m., revealed no sugar. By this time she had exceeded the limits of time allowable in hospital and she was discharged still uncontrolled, but with a fasting blood sugar value almost within the normal range. Her urine remained free of acetone, and she put on nearly 12·6 kilograms (two stone) in weight during her stay in hospital. She returned to the clinic for further observation. Her dose of protamine zinc insulin was finally increased to 100 units in the morning, and she was given 40 units of standard insulin at night, and her diet was reduced in fuel value from 1,800 Calories to 1,400 Calories. She felt well, but her records of her home tests showed abundant sugar in the urine. It was thought unwise to increase the dose of zinc protamine insulin further to an ambulatory patient of possibly uncertain reliability, so the use of this substance was finally abandoned, and she returned to treatment by standard insulin in doses of 40, 20 and 40 units per day. Her urine became sugar free within one week and has remained so to all her home and clinic tests for the past two months, though her dosage of insulin has been altered to 45 units of standard insulin twice a day.

CASE VII (see Figure VI).—H.McG., a female, aged fifty-five years, first attended the clinic in September, 1937. Examination of her urine showed 3% of sugar and her fasting blood sugar content was 290 milligrammes per 100 cubic centimetres. She was immediately given

a diet with a fuel value of 1,600 Calories, and 10 units of standard insulin were given night and morning. The dose was gradually increased till she was taking 40 units of standard insulin twice a day; all her urine tests still showed 3% of sugar. At this time, eight months after her first attendance, her fasting blood sugar content was 186 milligrammes per 100 cubic centimetres. One month later it was decided that she would be a suitable patient for treatment with zinc protamine insulin, and she was given 70 units of zinc protamine insulin *plus* 25 units of standard insulin. All specimens of urine examined still contained 3% of sugar and her fasting blood sugar content was 280 milligrammes per 100 cubic centimetres. The dose of insulin was raised in steps of 10 units at a time until she was taking 110 units of zinc protamine insulin *plus* 50 units of regular insulin. Even this failed to lessen the amount of sugar in her urine. At the sites of injection of the zinc protamine insulin small pea-like irritable and painful lumps arose. Standard insulin (Burroughs Wellcome and Company) had no such effect, so it was decided to replace the zinc protamine insulin entirely with this preparation.

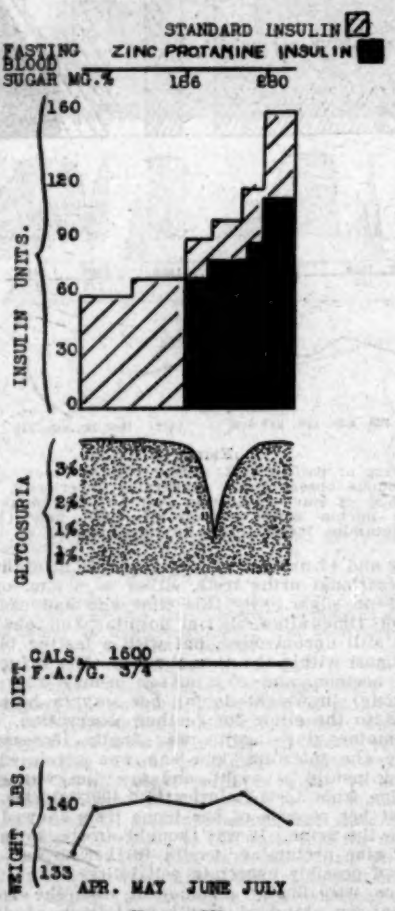

FIGURE VI.

Graph showing complete failure of control of an "insulin waster".

Deaths.

The following protocols are of the two patients who have died since treatment with zinc protamine insulin was commenced, one of pulmonary tuberculosis and the other of possible hypoglycæmia or cardiac disease, or both.

CASE VIII.—D.M., a female, aged forty years, first experienced diabetic symptoms after influenza, in May, 1936. She was extremely emaciated and remained so during the whole period of her attendance at the clinic. There was a family history of diabetes. On her initial visit her cerebration was considered to be somewhat unsatisfactory. She had a boil on her face and some œdema of the ankles. No particular abnormality was discovered in her cardio-vascular system. The result of urea concentration tests was satisfactory. Her fasting blood sugar content was 464 milligrammes per 100 cubic centimetres and reached 674 milligrammes two hours after the administration of 50 grammes of glucose. An electrocardiogram showed no departure from the normal. She was given immediate treatment with 10 units of standard insulin twice a day and a diet with a fuel value of 1,600 Calories (70 grammes of protein, 80 grammes of fat and 150 of carbohydrate). From then on at every visit her urine contained 2% of sugar. The results of her home tests were similarly unsatisfactory. The dose of insulin was increased over a period of three weeks to 40 units a day in two doses of 20 units each. She then deserted the clinic, but returned almost a year later, after a period of in-patient treatment. She had been admitted with considerable swelling of the legs, loss of weight and a suspiciously dark patch on the right great toe. She complained bitterly of pains in the legs. After a short and ineffectual trial on 45 units of regular insulin a day she was ordered zinc protamine insulin in a dose of 30 units in the morning and 10 units of standard insulin at night. This failed to control her glycosuria, and she was finally discharged on a diet of 1,400 Calories and 20 units of standard insulin a day. Following this she attended the clinic weekly and on each occasion had over 2% of sugar in the urine. She was retransferred to zinc protamine insulin alone in a dose of 50 units in the morning; this was increased to 80 units in two doses of 40 units each. She confessed to not having eaten all her food, but nevertheless had had no insulin reactions. On her last attendance she stated that she had been in bed, had not tested her urine, nor attended to her diet, as she had been considerably upset by the sickness of a nephew. Our next information about her was that she had been found dead in bed. Whether death had occurred from hypoglycæmic shock or from sudden cardiac failure it was impossible to determine, but in view of her anorexia the former was considered more likely.

CASE IX.—J.H., a male, aged fifty-two years, presented himself for treatment in February, 1938. He was thin and looked ill. His pulse rate was 110 per minute, and there were signs of spreading tuberculous infiltration in the upper lobe of each lung. The fasting blood sugar content on admission was 250 milligrammes per 100 cubic centimetres. He was given 25 units of zinc protamine insulin as an initial dose and a diet with a fuel value of 1,800 Calories (70 grammes of protein, 90 of fat and 175 of carbohydrate). He was referred to the anti-tuberculosis dispensary. This amount of insulin was sufficient to control his glycosuria; but his general condition deteriorated, he became bedridden and died one month ago.

Commentary on Results.

Success in diabetic therapy is difficult to define. Rosenthal and Finkelstein's standards (*vide supra*) may be obtained in one period of twenty-four hours; but the following day may be marked by hypoglycæmia. In such an instance it is open to question whether in the end the average blood sugar content of patients treated with zinc protamine insulin is nearer normal than that of patients receiving standard insulin only. Enthusiasts for the "Hagedorn era" must take notice of the fact that in the largest American series only 20% of 1,250 results are "excellent", while 60% are good. Our own figures, an incomparably smaller series, how-

TABLE II.

Synopsis of Patients and Results of Treatment.

Number.	Initials.	Age in Years.	Former Dose (Standard Insulin) in Units.	Whether Stabilized on this Dose.	Dose of Zinc Protamine Insulin (Units).		Dose of Standard Insulin.		Total Dosage of Both Insulins.		Time Required for Stabilization. (Weeks.)	Calories and Grammes of Carbohydrate per Day.	Results and Remarks (as Judged by Continuous Observation of Urine Tests).
					Initial.	Present.	Initial.	Present.	Initial.	Present.			
1	G.M.	37	—	—	35	70	10	60	45	130	14	1,800 (175)	Good. Has peroneal muscular atrophy. Admitted in hypoglycæmia within two weeks of apparent stabilization.
2	A.S.	44	45	Yes.	35	20	—	15	35	35	8	2,000 (172)	Excellent.
3	J.B.	20	—	—	30	125	30	15	60	140	12	1,600 (149)	Fair.
4	B.E.	19	60	Yes.	70	120	—	—	—	120	5	1,200 (92)	Poor. Now has diabetic neuritis.
5	A.Mc.	55	70	No.	70	110	25	50	95	165	—	1,600 (110)	Poor. Still uncontrolled after six weeks' treatment. Zinc protamine insulin caused local swelling, not so standard insulin.
6	W.W.	60	—	—	15	28	—	—	15	28	2	1,200 (115)	Good. No hypoglycæmia. Has had glycosuria at only two out of ten visits.
7	J.B.	10	20	Yes.	25	25	—	—	25	25	1	1,800 (172)	Fair. Frequent mild hypoglycæmia. No loss of tolerance observed on transfer from old to new insulin.
8	M.J.	50	40	Yes.	50	45	—	18	50	63	6	1,800 (125)	Good. Frequent mild hypoglycæmia.
9	I.S.	48	40	No.	30	30	15	—	45	30	1	1,400 (93)	Excellent.
10	K.G.	13	20	Yes.	20	90	—	—	—	90	—	2,000 (190)	Poor. No hypoglycæmia, but continuous hyperglycæmia and glycosuria.
11	N.M.	13	—	—	40	80	10	25	50	105	6	1,600 (135)	Stabilization delayed by coryza.
12	P.A.	10	—	—	10	15	—	—	10	15	1	1,800 (172)	Good. Occasional hypoglycæmia.
13	A.M.	24	20	Yes.	15	25	—	—	15	25	3	1,800 (175)	Excellent. No hypoglycæmia nor glycosuria.
14	D.M.	41	60	No.	50	—	—	—	50	80	—	—	Found dead in bed. Also known to have myocardial degeneration.
15	M.W.	25	80	No.	50	60	25	25	75	85	3	1,800 (125)	Good.
16	J.H.	52	—	—	25	30	—	—	25	30	2	2,000 (193)	Good, but died of pulmonary tuberculosis.

TABLE II.—*Continued.*

Synopsis of Patients and Results of Treatment.—Continued.

Number.	Initials.	Age in Years.	Former Dose (Standard Insulin) in Units.	Whether Stabilized on this Dose.	Dose of Zinc Protamine Insulin (Units).		Dose of Standard Insulin.		Total Dosage of Both Insulins.		Time Required for Stabilization. (Weeks.)	Calories and Grammes of Carbohydrate per Day.	Results and Remarks (as Judged by Continuous Observation of Urine Tests).
					Initial.	Present.	Initial.	Present.	Initial.	Present.			
17	M.R.	68	10	—	10	20	—	—	10	20	4	1,600 (97)	Good.
18	T.P.	46	20	Yes.	15	35	—	—	15	35	2	2,000 (139)	Good.
19	W.M.	18	65	No.	40	60	20	—	60	60	—	2,200	Poor. A former insulin waster. No improvement in seven weeks, but attendance unsatisfactory.
20	A.H.	48	78	No.	30	35	15	30	45	65	—	1,800 (172)	Poor. Frequent hypoglycæmia at inconstant times of day prevents further increase in dose.
21	L.W.	14	20	No.	20	25	8	8	28	33	4	1,800 (172)	Good.
22	M.F.	73	10	No.	20	20	—	—	20	20	2	1,600 (107)	Fair. Anxious type.
23	O.H.	34	35	Yes.	20	40	26	33	46	73	4	2,000 (142)	Fair. Anxious type.
24	M.S.	64	15	Yes.	20	20	—	—	20	20	2	1,400 (93)	Good.
25	M.M.	77	12	Yes.	12	12	—	—	12	12	1	1,600 (107)	Good.
26	J.McQ.	19	30	No.	30	45	10	5	40	50	4	1,800 (175)	Fair. Stabilization delayed by tonsillitis.
27	B.R.	20	100	Yes.	50	100	—	40	50	140	—	1,400 (93)	Has reverted to standard insulin with much better result.
28	H.S.	62	50	Yes.	50	40	—	—	50	40	2	2,200	Fair. No hæmochromatosis.
29	A.L.	59	—	—	10	16	5	—	—	16	2	1,600 (97)	Good.
30	S.G.	55	10	No.	15	30	—	—	—	30	6	1,400 (93)	Excellent. Only one mild hypoglycæmic attack in six months, and urine entirely free from sugar.
31	F.B.	44	—	—	20	30	—	—	20	30	2	1,600 (110)	Good.
32	A.M.	19	30	Yes.	25	25	5	7	30	32	2	1,800	Good.

ever, are: excellent, 4; good, 15; fair 6; poor, 7. Could not this proportion be approached in the "Banting era"? Our experience would suggest that it could.

Summary and Conclusions.

1. A series of 32 diabetic patients have received zinc protamine insulin for upwards of three months. These patients were in some part deliber-

ately chosen because of difficulty of control with standard insulin, but also chosen so as to constitute a representative cross-section of the diabetic community. In general, the immediate results were clinically satisfactory. Even where results were classed as "fair", the patients increased in weight and strength. Control can be arbitrarily stated to have been excellent in four cases, good in 15, fair in six and poor in seven, including two in which return to ordinary insulin was made, with subsequent improvement.

2. The hyperglycæmia of intelligent ambulatory diabetics can be controlled by suitably chosen doses of zinc protamine insulin, supplemented, if necessary, by smaller doses of standard insulin.

3. The best results, judged according to satisfactory control of glycosuria without disturbance of the patient's comfort by hypoglycæmic reactions, are obtained in individuals, usually adults, formerly requiring, or such as would require, two small injections not exceeding a total of 30 units of standard insulin a day.

4. Zinc protamine insulin in larger doses is a less satisfactory method of treatment in severe diabetes, but theoretically should result in a better average level of blood sugar throughout the twenty-four hours than obtained by smaller repeated doses of standard insulin. Its application is, however, frequently punctuated by the sudden and unexpected development of hypoglycæmia, for which no satisfactory explanation, beyond vagaries in the rate of absorption, can at present be offered. Such attacks appear without warning, and so do similar obscure periods of glycosuria. Their appearance unfortunately tends to undermine the vitally important confidence of the patient in his ability to lead a "normal" life, and is frequently a temptation to make sudden changes in diet arrangement or insulin dosage, which, having regard to the long latent period before the full effects of such a change are apparent, render the whole therapeutic technique more difficult than formerly, with more frequent recourse to blood sugar estimations. Frequent hypoglycæmia means frequent sugar therapy, with subsequent hyperglycæmia. Unless this can be relieved by careful insulin and diet adjustment, the net result in these patients is doubtfully superior to that obtained by the use of standard insulin.

5. The lowering of the post-prandial blood sugar peaks, and the generally closer approach of the carbohydrate metabolism to normal, are probably the most important consideration from the standpoint of progressive arterial degeneration, and may render persistence in this form of treatment worth while in spite of the above disadvantages, as much careful laboratory research has proved zinc protamine insulin to be superior in this respect to standard insulin.

6. Successful control by zinc protamine insulin of a patient previously satisfactorily treated by standard insulin does not often mean a reduction in insulin dosage or expense, though the number of injections can usually be reduced to one per day.

7. We seem to have experienced less difficulty and observed fewer hypoglycæmic disturbances when patients have been treated *ab initio* with zinc protamine insulin, although a longer interval than usual must pass before the patient becomes completely aglycosuric.

8. It is to be understood that the results of treatment of such a small series of patients cannot present any final decision as to the value, especially the remote value, of the new insulin; but sufficient time and thought have been accorded our first results to permit of a stocktaking.

9. In summary our provisional impression is that zinc protamine insulin: (*a*) is ideal for patients with mild diabetes requiring insulin, mostly elderly diabetics; (*b*) is a great boon to nervous patients who dread hypodermic injections; (*c*) is an advantage when dealing with the "diet-breaker", ensuring a more constant availability of insulin; (*d*) is less satisfactory in the treatment for moderately severe diabetes, which demands more careful medical and laboratory supervision and an average grade of intelligence on the part of the patient; (*e*) exposes the patient with severe diabetes to sudden and severe hypoglycæmia; (*f*) in our limited experience has not eliminated the problem of the "insulin waster".

Appendix.

Additional Instructions for Patients Taking Zinc Protamine Insulin.

(Diabetic Clinic, Royal Prince Alfred Hospital.)

This new form of insulin begins to act later, but has a more lasting action than the old, so that in suitable cases only one injection a day need be given, either just before breakfast or tea, according to the doctor's instructions.

The insulin is usually of double strength, and should be cloudy, not clear like ordinary insulin. It must be shaken well before use. The syringe must be rendered perfectly free of spirit and is best boiled beforehand. If a discoloration or crust forms inside the syringe it can be dissolved by vinegar or dilute acetic acid.

It is often ordered that some ordinary insulin should be given along with the zinc protamine insulin. This should be given separately and into a separate place, with another needle.

The diet is rearranged for the new insulin—breakfast is the meal containing least of the starchy foods, and afternoon tea and especially supper must be taken regularly.

The time for insulin reactions is usually in the late afternoon or early evening, or in the night if large doses are taken. The attacks are like those which occur with ordinary insulin, and no more dangerous, but they sometimes tend to come back an hour or two later. You may have only a feeling of slight shakiness or of feeling chilly, so it is well to be ready for them then. You must explain the possibility of these attacks and their treatment to your family. If you are about to do a hard day's physical work, the effect of exercise should be allowed for in the dose. Some carbohydrate should be taken before unusual exercise.

The urine is to be tested as usual, but the times are a little different. Thus: (i) on waking; (ii) just before breakfast—say one hour later than the first specimen; (iii) 11 a.m.; (iv) 4 to 5 p.m.; (v) bed-time—9 to 11 p.m.

If you are sick and showing lots of sugar, the dose of standard insulin is to be increased rather than that of the zinc protamine insulin, but preferably report to the clinic as soon as possible for advice.

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IMMEDIATE FEEDING IN HÆMATEMESIS AND MELENA: A REVIEW AFTER TWELVE MONTHS' TRIAL.

By J. D. HEALEY, M.B., Ch.M.,
Honorary Physician, Lewisham Hospital, Sydney.

BLOOD transfusion, as a method of treatment in hæmorrhages due to peptic ulcer, was at one time regarded with fear, and it was not considered a wise method to adopt, except as a preparatory measure for immediate surgery. With this bogy not so long ago relegated to oblivion, an equally great advance has made its appearance in the field of medical treatment, namely, immediate feeding.

Meulengracht, who advocated this method, published results showing not only how "harmless" it was, but also how much more favourable was the mortality rate compared with rates recorded to date by investigators following any other method of treatment.

The old routine method, quite frankly styled "starvation treatment" by those patients who had experienced it, had never appealed to the thoughtful physician. The main objections to the medical mind were that it was far too irksome, and that, in most cases, the attempts to replace the depleted body fluids were so often hopelessly futile. The greatest objection was, however, that the physician was expected to carry out a routine conflicting with one of the main principles of treatment—that is, "resting the stomach". It is well known that hunger peristalsis is most severe; and one of the aims of frequent small meals is to reduce these movements to a minimum. In the more severe cases especially, this old routine produces unsatisfactory results in all directions, and at times results in a patient, rapidly declining in mental and physical condition, being advised that surgical interference is his only prospect of recovery. It is remarkable that the "starvation routine" still holds sway, despite its many drawbacks and its poor results, when a method is open to trial which is likely to produce better results.

To break away from conservatism is not always easy; but the necessary moral support was forthcoming with Meulengracht's article, published in *The Lancet*, and later on with Professor Witts's article (*vide The British Medical Journal*, April 24, 1937, page 847).

For over twelve months I have employed Witts's modified Meulengracht routine, which appealed to me as being perfectly safe and not so iconoclastic as the original. Being at one and the same time a judicious blending of the best features of the Meulengracht and the Sippy methods, it fulfils all the other requirements of treatment.

My results to date in the treatment of both private and hospital patients have been distinctly encouraging. So far there has been no occasion to invoke the aid of the surgeon; but I am satisfied that, should this need arise, the surgeon would be offered a reasonably good risk, and not a forlorn hope as in the past. Previously the surgeon's aid was sought for the patient completely debilitated, generally as well as locally. Today, however, we can be quite confident that surgery is required only when thorough medical treatment fails.

Many physicians may be apprehensive; but when they consider the two reports published in 1936, which record the best medical and the best surgical results to date, the comparison should encourage them to throw aside the old and embrace a new method of distinct promise.

The best medical report comes from Meulengracht, who records a series of two hundred and seventy-three quite unselected patients with hæmatemesis and melena, all treated by immediate feeding, with a mortality rate of 1%. The best surgical report is from Finsterer, who records a 5% mortality rate for immediate operation, and a 30% mortality rate for late operation, in bleeding peptic ulcer.

It is no wonder, then, that Professor Witts naïvely remarks that Finsterer is an exceptional surgeon; and while it is asking too much to expect the average surgeon to be a Finsterer, every physician should be able to carry out Meulengracht's simple method.

Seeing that solitary hæmorrhages are rarely fatal (in about 4% of cases), and that with recurrence the mortality rate rises to 40% (with further

hæmorrhages, to 60%), the key to the situation is to prevent such happenings. The treatment, in short, should therefore be as follows: (i) the exhibition of morphine; (ii) blood transfusion; (iii) administration of food and fluids; and (iv) the administration of ten cubic centimetres of "Clauden" by intramuscular injection. I shall discuss these *seriatim*.

I. Morphine should be used only when anxiety is a prominent feature.

II. Blood transfusion should not be regarded purely as a preparatory measure for surgical interference. Results to date appear to indicate that medical treatment will improve by its adoption. We have in it the appropriate method for restoration of the blood volume, and it is free from danger if skilfully carried out. As a routine measure it is not employed; but we are always guided by the following conditions: (*a*) a systolic blood pressure below 90 millimetres of mercury, (*b*) a pulse rate of 140 beats or more per minute, (*c*) a blood urea content of more than 100 milligrammes per 100 cubic centimetres (any reading over 80 milligrammes is considered to indicate severity), and (*d*) a hæmoglobin value of less than 40%.

It is always essential to treat the general condition of the patient and not to concentrate on one symptom alone. After blood transfusion a rise in the hæmoglobin percentage occurs. Thus is eliminated the state of anoxæmia, and a condition is created which directly aids healing and must therefore tend to prevent a recurrence of bleeding. Should further hæmorrhages occur, the blood transfusion should be repeated as often as is necessary, preferably by the continuous drip method.

III. With a hæmorrhage and its associated vomiting *et cetera*, the patient probably loses between 2,000 and 3,000 cubic centimetres of body fluid. As the normal water requirements of a patient are 3,500 cubic centimetres per day, it is evident that he requires about 6,000 cubic centimetres during the first twenty-four hours in order to make up the leeway. This should be followed, each subsequent day, with 3,500 cubic centimetres. Under the old method the patient received much less than this, and thus remained in a dehydrated and collapsed condition; many patients, indeed, remained uræmic. With Witts's modified routine the water loss is readily overcome.

The rigid withholding of food by mouth is a further distinct fault in the old method for two main reasons: (*a*) a patient in danger of dying from exhaustion must be provided with a diet containing sufficient calories and also vitamins, and (*b*) to allow a stomach to remain empty and exposed to the unbuffered gastric juices is incorrect treatment of peptic ulceration. Why, then, promote excessive stomach movements as the result of hunger? The food must be kept moving through the stomach in order to rest it. Immediate feeding with a bland diet is, therefore, at least logical.

Following Witts's diet routine, which gives more fluid than Meulengracht's, the patients treated so far have received 2,500 to 3,500 Calories per day and a total fluid intake of at least 2,500 cubic centimetres. In addition, between meals, they were allowed water or glucose solution. The milk was not citrated, but if desired was flavoured with "Horlick's Malted Milk" or "Ovaltine". Alkaline powder and belladonna were seldom found necessary, but were given when required in the usual manner. Purgatives and enemata were avoided. Paraffin oil, however, was given when necessary. Constipation did not appear to upset these patients.

Vitamins were provided in the form of "Marmite", orange and tomato juice, cod-liver oil and malt. These were given at first in full doses to overcome any possible storage deficiency, especially of vitamin *C*.

According to the progress made, and when it was certain that bleeding had ceased, the gradual transfer to a modified Sippy diet followed. The original diet table as suggested by Witts has been used to date.

The following are brief notes of three of the more severe cases occurring among the hospital class of patient.

Case Histories.

CASE I.—W.M., a male, aged twenty-nine years, a mechanic, was admitted to hospital on October 19, 1937. He had collapsed four days previously. He sweated and was unconscious for fifteen minutes, and vomited dark red blood. He had had epigastric pain for two years. It had been dull in type, and occurred one and a half hours after food. He had been treated for peptic ulcer four months previously.

On examination he was extremely pale and weak, very anxious and dehydrated. Examination of the stools revealed melena. Examination of the blood revealed that the erythrocytes numbered 1,800,000 per cubic millimetre, the hæmoglobin value was 24%, the leucocytes numbered 11,650 per cubic millimetre. Five hundred cubic centimetres of citrated blood were given by transfusion and immediate feeding was begun. No alkalis and no belladonna were given. The bowels were well open naturally on the seventh day after admission to hospital. Full dosage of iron and ammonium citrate was given.

An X ray examination, four months earlier, had revealed the presence of a duodenal ulcer. After three weeks' treatment the X ray report was as follows:

> Small deformity at base of duodenal bulb; no delay in evacuation time of stomach.

Clinically, when the patient was discharged there was no evidence of activity, and he was put on a continuation diet.

CASE II.—Wm.C., a male, aged sixty-four years, was admitted to hospital on July 6, 1938, in a collapsed, uræmic condition. He was said to have passed a very large tarry stool twenty-four hours previously. In his early life there had been excessive drinking, but not for the last twenty years.

He had never had indigestion, but it was learnt on inquiry that he had suffered from pain across the lower part of the chest, and for two years had passed tarry, black motions at times. There had been no vomiting at any stage.

His illness was considered to be melena due to duodenal ulcer, the possibility of hepatic cirrhosis being kept in mind. Nephrosclerosis was a complication.

On July 7, 1938, the hæmoglobin value was 29%, the erythrocytes numbered 1,740,000 per cubic millimetre, the colour index was 0·85. The leucocytes numbered 22,550 per cubic millimetre, of which 86% were neutrophile cells, 13% were lymphocytes, and 1% monocytes. The blood urea content was 214 milligrammes per 100 cubic centimetres.

On July 7, 1938, a blood transfusion was given by the drip method; 1,200 cubic centimetres of citrated blood were given. The patient had been fed on the modified Meulengracht diet from his admission to hospital. He was still confused, and had a slight uræmic convulsion. An intramuscular injection of 10 cubic centimetres of 25% magnesium sulphate solution was given.

On July 9, 1938, he had a further large melena stool, the last portion consisting of bright blood. He was still retaining liquid and food by mouth, and the uræmic condition was still present. Ten cubic centimetres of "Clauden" and a further intramuscular injection of magnesium sulphate were given. A further 700 cubic centimetres of citrated blood were given by transfusion.

The patient continued to progress under this treatment. There was no further melena, and he became daily less confused. A final diagnosis of duodenal ulcer was made. An X ray examination later confirmed the diagnosis.

CASE III.—Mrs. M.A., aged fifty years, was admitted to hospital on November 10, 1937. A hæmatemesis had occurred at 1 p.m. on that day. For four weeks past she had suffered from anorexia and lassitude. Epigastric pain and a sensation of fullness after meals had been present during the past seven days.

Her appendix had been removed twenty-five years earlier. Five and a half years earlier she had been treated for duodenal ulcer. She had had a hæmatemesis two years earlier, when she was treated by the starvation method. Skiagrams taken three weeks afterwards had revealed a small ulcer in the lesser curvature of the stomach, towards the posterior wall, and just above the *incisura angularis*, with a spasmodic incisura on the great curvature at the same level. Evacuation time of the stomach was normal.

A fractional test meal was given with the following results:

	½ hour.	¾ hour.	¾ hour.	1 hour.	1½ hours.
Free acid ..	0·20%	0·27%	0·22%	0·30%	0·35%
Total acid ..	0·33%	0·37%	0·34%	0·46%	0·45%

On examination the patient was seen to be a thin woman who had obviously lost weight. Her expression was very anxious. She was extremely pale, sweating, tremulous and dehydrated. Examination of the heart revealed tachycardia, with heaving of the precordium; pronounced auricular fibrillation was present. She had a swelling in the right lobe of the thyreoid gland.

A blood count revealed that the hæmoglobin value was 43%, the erythrocytes numbered 2,370,000 per cubic millimetre, and the colour index was 0·89. The leucocytes numbered 14,000 per cubic millimetre, of which 65% were neutrophile cells, 1% were eosinophile cells, 30% were lymphocytes, and 3·5% were monocytes. The urea content of the blood was 43 milligrammes per 100 cubic centimetres.

In the first twenty-four hours the patient had twenty melena stools.

Ten cubic centimetres of "Clauden" were injected into the buttock. A transfusion of 600 cubic centimetres of citrated blood was given and an immediate start was made with the modified Meulengracht diet. The thyreotoxicosis was a nasty complication, and subsided *pari passu* with the improvement of the gastric condition.

An X ray report on December 6, 1937, was as follows:

> There is still a small ulcer crater on posterior wall and towards lesser curvature side of middle one-third of stomach, with a large incisura on greater curvature immediately opposite it. No delay in evacuation time.

When the patient was discharged the thyreoid enlargement had almost disappeared. She was given iron *et cetera*.

This patient is interesting, as she can testify to the improvement in treatment by feeding, in contrast to the treatment she had received two years before.

Summary.

1. Immediate feeding in bleeding peptic ulcer appears to be a decided advance in treatment.
2. The outlook for and the immediate comfort of the majority of these patients are now distinctly improved.
3. Although bleeding in certain cases will take place whether the patient is fed or not, it has been shown that most patients respond to present-day medical treatment by immediate feeding, with blood transfusion when necessary.
4. The treatment is well within the compass of all physicians.
5. Should surgery become necessary, the patient is in a much better physical condition to stand up to his ordeal than he was after the old methods.

Reports of Cases.

LOCAL ANÆSTHESIA FOR RETROSTERNAL GOITRE.

By T. MAYNARD FURBER,
Sydney.

LOCAL analgesia seems to make but slow progress amongst practising surgeons, and its frequent life-saving qualities do not seem to be adequately appreciated.

Dr. C. E. Corlette has on numerous occasions drawn attention to the cases in which local analgesia is indicated, and has pointed out that the technique is easily acquired and has shown that the procedure is eminently safe. Although some of the seed has taken root in the favourable soil of the minds of the younger men, it still seems disappointingly long before the public at large can benefit by the added safety ensured in a number of cases by a method which, though it takes more out of the surgeon, returns priceless dividends of safety for the investment of this small amount of extra mental energy.

The case reported below seems worthy of record, partly because the disorder is uncommon, but mainly because local analgesia made quite safe and easy an operation which, under general anæsthesia, would have been very hazardous.

The patient was a woman, aged forty-eight years, who for ten years had had a swelling in the neck which had been increasing in size for the last year. In April, 1938, she was treated at the out-patient department of the Royal Prince Alfred Hospital for shortness of breath on exertion, a feeling of tightness in the throat and nervousness. Investigation at that time showed no thyreotoxicosis, and her symptoms were relieved by medical treatment.

She remained well till October 3, 1938, when, after a bout of coughing, she felt a severe dragging pain in the upper sternal region and in the left side of the neck, a feeling of suffocation and difficulty in getting her breath, difficulty in swallowing and weakness and softness of the voice.

Dr. W. C. McClelland, who was called to her, thought that a hæmorrhage had occurred into a thyreoid cyst, and arranged for her admission to the Royal Prince Alfred Hospital.

When I saw her on the afternoon of October 4, 1938, about twenty-four hours after the onset, her general

appearance was one of intense and anxious concentration on getting enough breath in; there was quite pronounced inspiratory stridor with epigastric and slight suprasternal recession, a picture which immediately took one back to the old days of laryngeal diphtheria at the Coast Hospital. The voice was weak and husky. Behind the left sterno-clavicular joint there was a fixed, slightly tender mass, which, though it did not move on swallowing, seemed to be part of the thyreoid. Laryngoscopic examination showed that the left vocal cord was immobile, but as the larynx was otherwise normal, this was not enough to cause the respiratory distress.

It was considered that hæmorrhage had taken place into a retrosternal thyreoid cyst and had caused pressure on the trachea, œsophagus and the inferior laryngeal nerve, at the inlet to the thorax, which will accommodate comfortably only its normal contents.

The patient felt that she was becoming worse, and had that look of fear and appeal for help so characteristic of patients with respiratory obstruction, so it was decided to do something to relieve the pressure.

The question of anæsthesia immediately arose, and it was recognized that the only safe way to give a general anæsthetic was to pass a tube past the obstruction. This I thought hazardous on account of the possibility that the trachea after long continued pressure had collapsed, on account of the absorption of the cartilaginous rings, into a state of scabbard trachea.

Safety manifestly lay in the plan of opening down to the cyst under local analgesia and evacuating the contents; then, being guided by the conditions found, one could decide on further action and anæsthesia.

A hypodermic injection of 0·015 gramme (one-quarter of a grain) of morphine and 0·004 gramme (one one-hundred-and-fiftieth of a grain) of hyoscine was given, and when the patient came to the operating theatre she had lost the look of fear and was much calmer.

Her distress was increased by lying down, so the operation was started in the sitting position after both cervical plexuses had been blocked. The analgesia was perfectly satisfactory till it was necessary to invade the mediastinum, which had not been anæsthetized.

The pre-operative diagnosis was confirmed, and it was found that the goitre extended down further than could be felt, and that the end was bulbous and so impossible to deliver through the thoracic inlet. A cavity with rough shaggy walls was opened into through normal-looking thyreoid tissue just above the clavicle, and was found to contain about three ounces of black clot and to extend from just above the clavicle down into the mediastinum further than I could reach. As soon as the clot was got rid of she said she could breathe freely.

I had to stop trying to shell the tumour out of the mediastinum, which had not been anæsthetized; so, as it was now quite safe, Dr. Charlton gave enough open ether to allow him to pass a Magill's tube through the nose into the larynx and carry on with ether and oxygen. The patient was then laid flat and the retrosternal tumour was easily delivered and removed.

Exploration of the cavity left in the mediastinum after removal of the cyst showed that it extended about ten centimetres (four inches) below the suprasternal notch. On its left side were the aortic arch and the origin of the common carotid artery (this was apparently where the inferior laryngeal nerve was compressed), and on the right side the cavity passed behind the trachea quite five centimetres (two inches) across the middle line, thus pressing the trachea forward against the sternum.

It could be seen that in the lower pole of the specimen there was a cyst into which bleeding had occurred, and that the blood had burst the cyst and ploughed its way upward, thus causing the shaggy cavity from the upper end of which the clot was evacuated. Apparently there was plenty of room in the mediastinum for the goitre, and the hæmorrhage and pressure symptoms occurred only when the blood forced its way up to the thoracic inlet.

The post-operative period was uneventful, and the patient was discharged in a fortnight without symptoms and with a normal voice and both vocal cords moving.

The technique of blocking the cervical plexus is easy and safe, and in my experience the results have been very happy. I have followed the method of Labat, but have used 0·5% "Novocain" solution instead of 1% as he recommends, and have found this strength quite satisfactory. I have not found it necessary to give the large amounts (forty to fifty cubic centimetres) advised by Braun, ten cubic centimetres per nerve root being quite enough.

I understand that Dr. Corlette has written a book on local analgesia. This should prove a great help to those with sufficient mental elasticity and energy to want to learn new methods of making operations safer, and also to the younger men, particularly those in the country and those in "one-man" towns, one of which I recently visited. There I found that the method was appreciated at its full value and was in frequent use.

Reviews.

VARICOSE VEINS AND HÆMORRHOIDS.

"THE INJECTION TREATMENT OF VARICOSE VEINS AND HEMORRHOIDS", by Dr. H. O. McPheeters and Dr. K. Anderson, offers in one handy volume a complete résumé of these conditions.[1] The ætiology and pathology and the treatment, with its indications, are neatly discussed. The technique of injections is fully described. A plea is made for the more common application of injection treatment; for example, during pregnancy, when varices are painful and distressing, owing to their size. It is claimed that a more accurate control of the strength and localization of the solution injected will give a higher percentage of good and permanent results. For the general practitioner who indulges in the injection treatment of varicose veins and hæmorrhoids, this book will prove invaluable. It is beautifully illustrated.

PSYCHOANALYSIS.

IN his latest edition of "Papers on Psycho-Analysis" Dr. Ernest Jones displays the same knack of clear and restrained writing as was shown in his previous works.[2] Whilst he pays homage to Freud (to whom the book is dedicated), the debt is not one-sided. Undoubtedly the prestige and spread of psychoanalytical theory and practice owes much to this brilliant disciple of the master.

The book is a collection of papers written by Dr. Jones. In the four editions eighty papers in all have been published. The present volume omits twenty and includes twelve new ones. It is to be regretted that "More Recent Advances in Psycho-Analysis" has been omitted from this edition. Dr. Jones admits that he had not the time for such a laborious task, an admission which shows that even analysts are mortal. It is perhaps the most unfortunate end-result of this type of knowledge that the tiro is left with a too vivid realization of his own disabilities. He is uplifted to find that even the great are not immune. Psychoanalysis must be taken seriously, but not too seriously.

The book is divided into four sections: general papers, papers on dreams, clinical papers and papers on child study. The reader will be glad that a chapter deals with the psychopathology of everyday life. It treats of the trivial difficulties that beset even the erudite—forgetting, *lapsus linguæ*, *lapsus calami*, misprints, false

[1] "Injection Treatment of Varicose Veins and Hemorrhoids", by H. O. McPheeters, M.D., F.A.C.S., and J. K. Anderson, M.D., F.A.C.S.; 1938. Philadelphia: F. A. Davis Company. Medium 8vo, pp 315, with 82 illustrations. Price: $4.50 net.

[2] "Papers on Psycho-Analysis", by E. Jones, M.D., M.R.C.P.; Fourth Edition; 1938. London: Baillière, Tindall and Cox. Medium 8vo, pp. 654. Price: 25s. net.

visual recognition, mislaying of objects *et cetera*. Whilst the interpretations seem at times to be unduly complicated, there is little doubt that psychoanalysis sheds some light on these topics.

Discussing the future of psychoanalysis, Dr. Jones does not foresee any revolutionary changes in technique, but rather "a steady progress in thoroughness, a greater polish and accuracy leading to much more sureness than we now possess".

The short paper on cold, disease and birth deals with the pathological importance so universally ascribed to cold air. The author hints that this belief may be based on the suffering of the newly expressed fœtus which finds itself deprived of its warm nest and plunged into a cold unsympathetic atmosphere.

In this large volume there are papers on psychosexual impotence and anæsthesia, the psychopathology of anxiety, fear, guilt and hate, jealousy, some problems of adolescence, the significance of the grandfather, ano-erotic character traits, early female sexuality and other subjects. The volume contains a useful glossary of psychoanalytical terms.

For those who wish for an authoritative introduction to psychoanalysis, this book can be recommended. The best source is undoubtedly original papers, but the diversity of the presentation is in one sense a drawback, since it calls for previous experience of the matter in hand. Undoubtedly the best recommendation for this book is that it lives up to the high standard of its predecessors.

DISEASES OF CHILDREN.

A SECOND edition of Dr. Wilfred Sheldon's "Diseases of Infancy and Childhood" has appeared eighteen months after the first.[1] No radical change in the book has been made, but newer therapeutic methods, which were on trial in 1936, are now included. A useful appendix, containing the dosages for children of the most commonly used drugs, has been added. The chapter on intrathoracic tuberculosis has been recast and the question of the relationship between the hypersensitive state and immunity is discussed. This is one of the best features of a reliable and useful hand-book.

FORENSIC MEDICINE.

SYDNEY SMITH'S "Forensic Medicine" is now in its sixth edition.[2] As less than two years have elapsed since the issue of the fifth edition, there is no need to emphasize the popularity of this book, the first edition of which was issued in 1925. In the new edition the text has been revised in general, and several new illustrations have been added, while others have been replaced.

Writing of sudden death from natural causes, the author maintains that fatty degeneration of the heart and myocardial degeneration in general are the most common lesions which cause this catastrophe. In our experience the most common cause is disease of the coronary arteries and any associated myocardial change is more often fibroid than fatty.

More stress is laid upon the value of the blood test for alcoholism than in previous editions, the author stating that the time has arrived for the legal authorities to make more use of this test in connexion with cases tried under the *Road Traffic Act*, but he does not show how this can be done. Police or legal authorities have no power in Great Britain or in Australia to take blood for this test. In any case, we are sceptical of the reliability of the testing of a drop or two of blood. Sydney Smith writes that the Widmark method is essentially one for a skilled analyst. From the obviously incorrect figures published in medical journals from time to time, this is no doubt true. Some of Widmark's own figures are not free from suspicion. However, at an autopsy in a case in which death has been caused by a motor accident, blood or urine or both should always be taken for analysis.

Although there is as yet no laboratory test for sex, the author looks forward to an advance in knowledge of specific hormones which may provide such a test in the future. Analysis for poisons occupies more than fifty pages of the volume. This is not excessive comparatively, but we wonder whether in these times in a book written for students and practitioners it is necessary to describe analysis in full detail. A medical man is not now expected to make an analysis, which is rightly left to the expert chemist. However, there is little to criticize in this work. Possibly the distinguished author might consider adding to his next edition an appendix of a few coloured plates, more particularly illustrating the effect of poisons.

The book is ably written from a wide experience, and is finely illustrated. There is no better text-book of forensic medicine in the English language.

THE EUCALYPTUS ON PARADE.

RECENTLY several eminent members of our profession have lamented the advent of this age of speed and specialism. They have pointed out that the medical practitioner of yore, leisured and with wide interests apart from his profession, has had to give place to him whose hobbies are, for want of time, necessarily bound up with the furtherance of his medical knowledge and skill. "A Gallery of Gum Trees",[1] written by Dr. A. W. D'Ombrain, and illustrated by Miss Tydfyl Evans, is proof that some at least of the medical profession still have eyes to see. Dr. D'Ombrain states in his preface that his attention was first drawn to the enormous variety of eucalyptus trees as he went on his daily professional round in the Hunter River Valley. He sought a book from which he could learn about them. To his surprise, no book that was not too technical was to be found; so, on the principle that the best way to learn all about anything is to write a book about it, he determined to make one on gum trees.

The finished product does great credit not only to Dr. D'Ombrain, but also to the artist, Miss Tydfyl Evans, for her charming paintings of the trees, and to the publishers for their excellent craftsmanship. The book consists of a series of twenty-one coloured plates, each facing a brief, informative description of the tree portrayed. The artist has so arranged matters that each plate shows in detail each part of the tree; this object has been achieved by the inclusion of two, three or even more trees in each painting. The immediate effect of reading the book is to make the uninitiated eager to go forth in search of gum trees to identify them with its aid; we have tested it and found it eminently satisfactory. An unexpected but pertinent inclusion is a short chapter on the food habits of the koala. This involves some discussion of the chemical content of various types of eucalyptus leaves.

The book is artistically set up in brown ink on heavy buff paper and is well bound. Each of its illustrations is worthy of being framed. There is no doubt that it will admirably fulfil the purpose for which it was made.

[1] "Diseases of Infancy and Childhood", by W. Sheldon, M.D., F.R.C.P., with a foreword by Sir F. Still, K.C.V.O., M.A., M.D., LL.D., F.R.C.P.; Second Edition; 1938. London: J. and A. Churchill Limited. Demy 8vo, pp. 751, with 125 text figures and 13 plates. Price: 21s. net.

[2] "Forensic Medicine: A Text-Book for Students and Practitioners", by S. Smith, M.D., F.R.C.P., D.P.H., with an introduction by Professor Harvey Littlejohn, F.R.C.S., F.R.S.E.; Sixth Edition; 1938. London: J. and A. Churchill Limited. Demy 8vo, pp. 668, with illustrations. Price: 24s. net.

[1] "A Gallery of Gum Trees", by A. W. D'Ombrain, M.B., Ch.M., D.O.M.S.; 1938. Sydney: Australasian Medical Publishing Company Limited. Crown 4to, pp. 53, with illustrations from original paintings in water-colour by T. Evans. Price: 17s. 6d. net.

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HOW MUCH ANATOMY?

AN article entitled "The Medical Curriculum and Present Day Needs", which appeared in the issue of September 3, 1938, of *The British Medical Journal*, raises the perennial question, "How much anatomy?" The medical curriculum becomes increasingly complex as knowledge accumulates; how to make the training of the student adequate without overburdening him is a problem difficult of solution. The question of the amount of anatomy which the student should study may be examined from many aspects. There are the point of view of those who were brought up on Holden's text-book at least fifty years ago, the opinion of those who learnt their "bones" from Cunningham some forty years ago, and finally the ideas of the young and recent graduates. The majority of those who sit on councils convened to recommend changes in the medical curriculum will probably belong to the first two classes. Since the writer of the article to which we have referred, seems to suggest that with Holden's "Osteology" as a text-book it was difficult to make the dry bones live, and that the average student should not be taught too much detail because he cannot retain it, we would recall the experience of the Great War. In France the surgeons from Great Britain and Australia were celebrated for their anatomical knowledge. Men were called upon to operate on areas of the body in which they were not greatly experienced, for they were not all specialists. The teaching of the Holdens, Turners, Cunninghams, Lockwoods, Thanes, Wilsons and others had been thorough. These anatomists had guided their students through the complexity of the city of the human body and, although the names of the streets were forgotten, the important landmarks were familiar. We cannot afford to belittle the thoroughness of that old British school, to which Australian surgery owes much.

How much anatomy should be taught to medical students is regarded as a serious responsibility by the professorial staffs of the universities. This is emphasized in the article, for the writer says: "When we wished to lighten the curriculum, we found the anatomists steadfast, immovable, always abounding in the faith that dissection of the whole body is necessary to salvation." It is fortunate for the profession that the anatomist is steadfast; and it is always a healthy sign in any faculty of medicine that surgeons, gynæcologists, neurologists and others take an active part in the teaching of the subject in the anatomy departments. It brings home to the student not only that the human body is a unity in which the eye cannot say to the hand, "I have no need of thee", but that there is also a unity within the profession in which all the members have need one of another.

The question of how much anatomy should be taught is dependent, not so much on the amount of time that is available, not so much on any set method of teaching, and certainly not on considerations whether the student can remember or not, important as these things may be, as on the quality of the student. Reforms in medical education must begin in the schools. Before a student is allowed to embark on the medical course he should give

evidence of having had a good general education. To have been sickened with Shakespeare is of little value if the student is profoundly ignorant of the quality and the technique of descriptive English. There is no virtue in the passing of an entrance examination to a university if the subjects have been so painfully learnt that the student's only release from a noxious experience is to forget it as soon as possible. It is not a question of whether this or that subject should not be taught because the student might forget it, but of whether the methods of medical education in the British Empire, with their undue emphasis on the examination, are not taking the process of forgetting past the normal range into the pathological.

The examination system has evolved to such a degree that it is a bugbear both to examiners and to examinees. The idea that a child goes to school in order to be educated is often foreign to modern-day practice. It would sometimes seem that the sole object of school training is that an examination should be passed. There is little interest in any subject unless it is likely to prove useful in an examination. It is hardly an exaggeration to say that the pass list is sometimes used more for the promotion of the teachers and for the advertisement of the schools than for the benefit of the pupils. The student at such a school, having passed his university entrance examination, finds that he has committed himself to many years of grinding for further examinations. When he comes to the study of anatomy, he can think of it in no other terms than as an examination subject. All the efforts of his teachers to make the subject interesting are resisted, and he sets about trying to commit a prodigious feat of memory with a mind trained to "cram" and then to forget.

Whilst many condemn the examination system because its faults are only too apparent, no one can suggestive an alternative. The first step towards any reform in medical education is to improve the mental quality and cultural training of candidates for the profession. Students of inferior intellectual calibre become a drag on the progress of their fellows. Any subject can be studied at a high standard and with inspired enthusiasm by students whose cerebral equipment and school education have fitted them for the task.

Current Comment.

MECHANICS OF INTESTINAL OBSTRUCTION.

THE exact nature of the events that follow intestinal blockage and eventually lead to the death of the organism is still imperfectly understood. From the vast amount of research done on the subject, a number of hypotheses have emerged, none of them completely satisfying, and most of them rather too narrow to supply an explanation of all the changes seen in this condition. A fuller understanding of the fundamental changes produced by obstruction of the intestine is necessary before further progress in treatment becomes possible. With this end in view Louis Sperling has recently carried out a large series of observations on intestinal obstruction produced experimentally in dogs and cats.[1] Only simple obstruction was considered, the lower ileum being chosen as the site because little work has been done on obstruction in this region. Sperling's investigations were limited to the local changes in the gut wall, and included studies of the anatomical lesions, of the variations in motility and secretion, and of the phenomena of absorption from the obstructed gut.

Sperling's observations prove that the obstructed bowel, as well as increasing in diameter above the site of obstruction, shortens by contraction of its longitudinal muscle fibres, thus losing one-third of its original length. This shortening causes a greater increase in diameter, permitting the gut to accommodate a greater volume of contents. The bowel wall above the block gains in weight, partly owing to œdema, but mainly owing to the accumulation of blood in the vessels caused by venous stasis. Investigation of the bowel's tensile strength showed that the bursting pressure of obstructed gut was much lower than that of normal bowel. Sperling tried the effect of sustained intraenteric pressure upon closed ileal loops. He found that relatively low pressures (twenty to forty centimetres of water), such as are present in cases of intestinal obstruction, produced gross changes in the gut wall if sustained for twenty or thirty hours. Venous stasis and vascular engorgement occurred and were followed by hæmorrhage, necrosis and actual perforation.

The changes in motility and secretion were next studied. It was found that postural relaxation of the bowel above the obstruction permitted a great increase in the volume of the intestinal contents without much change in intraenteric pressure. Eventually, however, the pressure began to rise and

[1] *Archives of Surgery*, May, 1938.

peristalsis became increased. With high intraenteric pressure, spastic contraction, with intervals of relaxation, occurred. This is probably what happens in patients suffering from obstruction who complain of severe, intermittent, cramp-like abdominal pains. The amount of intestinal secretion was found to be greatly increased by distension; it was due partly to reflex causes and partly to increased diffusion from the capillaries.

Sperling's observations of absorption from the obstructed intestine showed that venous absorption of water and strychnine from the gut was greatly diminished after obstruction. Using dyes as an index, Sperling found that lymphatic absorption was increased after obstruction, apparently a result of the raised venous pressure. However, animals whose lymph channels had been ligated, died just as quickly of intestinal obstruction as those with normal lymphatics; hence there was no evidence that the increased lymphatic absorption was of lethal significance. Transperitoneal absorption of simple chemical substances is known to occur. Sperling showed that dyes and strychnine were unable to pass through viable bowel wall, but readily penetrated non-viable gut.

In his discussion of the probable lethal factors in ileal obstruction, Sperling states that loss of fluid and electrolytes by vomiting and by failure of the gut to absorb the normal amount of these substances is not so important as in high intestinal obstruction. The copious administration of saline solution will lengthen the survival period of animals suffering from jejunal obstruction, but has no effect on those with obstruction of the lower part of the ileum. Sperling considers that death is usually due to impairment of viability of the bowel wall, followed by transperitoneal migration of toxins and bacteria. He summarizes the events that follow low ileal obstruction thus: obstruction leads to intestinal stasis, distension, increased activity of the bowel and increased intraenteric pressure. The sequelæ to these are increased secretion of intestinal juices and diminished absorption, hence further distension. Eventually circulatory stasis occurs, causing anoxæmia of the gut wall and the consequent appearance of areas of hæmorrhage and necrosis, which are penetrated by toxins and bacteria. Death follows from toxic absorption and peritonitis.

Although Sperling's work reveals nothing startlingly new, it is nevertheless a useful contribution to the study of intestinal obstruction, because it places on a quantitative basis a number of changes that formerly were largely conjectural. One other point deserves mention in connexion with this subject, namely, the influence of the nervous system. It is reasonable to suppose that the inevitable, violent stimulation of visceral afferent nerves after the blockage of the intestine must have some general effect on the vegetative nervous system and, through this, on the vital functions. The work of Herrin and Meek is of significance. They found that distension of previously denervated loops of gut could be tolerated by animals almost indefinitely, without the production of anorexia, vomiting or dehydration. It seems likely that the nervous factor in intestinal obstruction is more important than has been thought hitherto.

DURATION OF ACTION OF ZINC PROTAMINE INSULIN.

In view of the divergence of opinion upon the duration of action of zinc protamine insulin during routine treatment, and hence upon the presence or absence of a cumulative effect, R. S. Aitken determined to make some precise observations upon a limited number of diabetics.[1] The method adopted consisted in the administration of the compound insulin to patients lying in bed whose sugar excretion on a fixed diet had reached a constant maximum. The duration of its action was taken as the time from the giving of the injection until the glycosuria, as estimated by Benedict's method, returned to its pre-injection level, or until the reappearance of acetone in the urine. Similar results were obtained by each method of reckoning. Aitken gives a cogent reason for lining the degree of glycosuria rather than the blood sugar concentration as his index. He states that as the fundamental purpose of insulin is to increase sugar utilization, an estimate of the sugar excretion is a more accurate index of this activity. His conclusions may be summarized as follows. The duration of action varies approximately with the dose. With doses of 50 to 100 units it can extend to 48 or even to 60 hours. Secondly, and this is most important, the duration of a given dose varies from patient to patient. In any given case it seems that the greater the carbohydrate intake, the longer the action of protamine insulin. The maximal effect appears to take place within three to six hours of the injection. Arithmetically, therefore, zinc protamine insulin given in large doses acts in a cumulative fashion, if administered once in twenty-four hours. This fact has been suspected by many users of the preparation, because of the severe hypoglycæmic attacks that may appear without warning under these circumstances. Aitken's findings suggest that recipients of more than fifty units of zinc insulin at a time should space their injections forty-eight hours apart, especially since the increase of glycosuria in the later periods is more gradual than its decrease in the earlier periods. This practice has actually been tried in America, but the general conclusion has been that the results are less satisfactory than injection every twenty-four hours. Time-course curves, as published by Aitken in his article, indicate that the best spacing of meals containing carbohydrate is usually at intervals of three hours. The observations recorded afford a valid guide to the clinical use of zinc protamine insulin.

[1] *The Lancet*, October 1, 1938.

Abstracts from Current Medical Literature.

PHYSIOLOGY.

A Special Form of Erythrocyte.

A. M. BARRETT (*The Journal of Pathology and Bacteriology*, May, 1938) has described a special form of erythrocyte possessing increased resistance to hypotonic saline solution. In stained films the cells are seen to have a darkly stained periphery and centre, and a pale intermediate zone, alternations of colour as in a target being produced. They are therefore called "target cells". These cells were observed in cases of obstructive jaundice in which resistance to hypotonic saline solution was present. The number of cells not hæmolysed by 0·3% saline solution was estimated, and also the percentage of target cells present in films from the sediment of a solution of blood in 0·3% saline solution. It was found that when the proportion of intact corpuscles reached 2% target cells were always present, but when the proportion was less than 2% they were almost entirely absent. As the jaundice faded the resistance to hypotonic saline solution and the number of target cells grew less. The blood of patients subjected to splenectomy was examined and it was found that target cells were absent at the time of operation, but appeared as the resistance to hypotonic saline solution developed. Experiments were designed to see if the target appearance was acquired during fixation, and it seemed as if that was so. Moist preparations were examined and many "bowl-shaped cells" were seen. Models of these were made in "Plasticine", and it was found that X ray pictures of these models gave the target appearance. Target cells were also found in the blood in hypochromic microcytic anæmia and in steatorrhœa. The authors discuss the mechanical theory of hæmolysis. They conclude that the resistance of a corpuscle is determined by the magnitude of its surface as compared with its volume, and that the resistance of the "bowl-shaped corpuscle" or "target cell" can be explained in this manner.

Diet and Resistance.

MARION WATSON, JOYCE WILSON AND W. W. C. TOPLEY (*The Journal of Hygiene*, July, 1938) have studied the effect of diet on epidemics of mouse typhoid due to *Bacillus typhi murium*. Two groups, each containing 100 mice, were fed on two different diets and exposed to contact infection by the introduction of 25 mice infected by intraperitoneal injection with uniform doses of bacilli. Mice fed on the diet containing dried skim milk, oatmeal and other constituents, proved to be more resistant than those fed on the diet from which skim milk was omitted. Not only was the mortality less in the former group, but there was also a reduced incidence of latent infection as judged by the presence of bacilli in cultures from the heart blood and the spleen of animals surviving after 60 days. Female mice appeared on the average to be more resistant than males to *Bacillus typhi murium*, but the sex difference in resistance was not constant.

Vitamin C Requirements of Man.

MARTIN HEINEMANN (*The Journal of Clinical Investigation*, September, 1938) has shown that at least 0·8 milligramme of ascorbic acid per kilogram of body weight is used daily by healthy subjects saturated with this vitamin. He states that smaller amounts maintain a lower concentration in the body stores. For protection against scurvy, 0·4 milligramme per kilogram, or even less, per day appeared to be sufficient. Abnormally high requirements were observed in patients with active tuberculosis and other diseases. Low concentrations of ascorbic acid were found in the blood of tuberculous patients despite a large intake of orange juice for some weeks previous to the estimations. Even lower concentrations were found in the blood of patients undergoing the Sippy treatment for peptic ulcer, and the diet supplied was shown to contain inadequate amounts of vitamin *C*. The author describes a comparatively simple method for the approximate estimation of the daily requirement of vitamin *C* as a clinical procedure.

Alanine and Growth.

J. KENNETH GUNTHER AND WILLIAM C. ROSE (*The Journal of Biological Chemistry*, March, 1938) have shown, by the use of diets devoid of protein, but containing mixtures of highly purified amino-acids, that alanine is a dispensable component of the food. Rats deprived of this amino-acid increased in body weight just as did controls receiving a similar ration supplemented with alanine.

Observations on Water Metabolism in the Desert.

E. F. ADOLPH AND D. B. GILL (*The American Journal of Physiology*, August, 1938) have studied the alterations in metabolism induced in human subjects, unused to hot conditions, by residence for some months at Boulder City, Nevada. The subjects were the members of the Harvard Desert Expedition. Studies of heat balances, chloride balances, blood changes and effects of exercise were made, and are recorded elsewhere. The present study deals only with water balances. The conditions of climate were such as to allow maximal rates of evaporation without the appearance of sweat upon the skin. The exposures during which perspiration was measured were ordinarily at the hottest part of the day and in direct sunlight. The mean shade temperature for these exposure periods was 35·3° C., with a maximum of 43° C. The mean humidity was 12%, and it varied from 6% to 30%. Radiation was usually undisturbed by clouds. Winds were relatively rapid, the mean velocity being 137 metres per minute throughout the twenty-four hours. Measurements indicated that output by evaporation increased eightfold or more, while the concentration of sweat decreased. The output of urine remained constant or else decreased, while the urine concentration increased. In exercise, rates of evaporation up to 1,600 cubic centimetres per hour were regularly found, and urine excretion rates down to 10 cubic centimetres per hour occurred whenever the urine became chloride-free. Intake of water was increased from three to six times, and was accurately adjusted to replace that lost by evaporation. The highest intake recorded was 7,370 cubic centimetres. The authors observe that while it is a distinct discomfort for a person in a winter climate to drink 4,000 cubic centimetres of fluids per day, it is a violent discomfort for a person in the desert to drink less. Ingestion lagged considerably behind output during exercise and was largely made up at meals. The rate of ingestion of water in man was slow in comparison with that in the desert burro, which drank water at a rate to restore its complete deficit within a few minutes. The water content (weight) of the body in human subjects was remarkably constant when measured at intervals of twenty-four hours.

Hormones and the Placenta.

W. H. NEWTON (*Physiological Reviews*, July, 1938) discusses the present position of our knowledge of the hormones elaborated by the placenta in human pregnancy. He remarks that a review of the literature published during the last few years reveals the placenta as a store of practically everything that is sought in it, including the male sex hormone, as well as the site if important enzymic processes. If it is assumed that every particular in which it differs chemically from other tissues denotes a corresponding functional activity, then the placenta, in point of versatility combined with simplicity of structure, easily outdoes the anterior lobe of the pituitary. The author observes that in many ways it seems to resemble the liver. He doubts whether it will be possible, for many years to classify and pigeonhole it as having a characteristic circumscribed function. The balance of evidence at present indicates that the placenta can produce œstrin, but there is little to show that it is responsible directly for the enormous amounts found in pregnant women. The evidence as to whether the placenta produces progestin is too scanty to be conclusive. With regard to gonadotropic substances, the association of trophoblastic tissue with the presence of large quantities of gonadotropic

substance in the body is unmistakable. There is still no direct answer to the question of whether these large quantities of gonadotropic substance or substances are secreted by the placental tissue itself or by the anterior lobe of the pituitary gland. This question is almost unanswerable, for hypophysectomy is unlikely to be performed on a pregnant woman, and would in any case almost certainly terminate the pregnancy. The author comments that it is ironical that the one hormone that would seem essential for pregnancy—progestin—is the least satisfactorily linked with the human placenta, while it is difficult to ascribe a function to the œstrin and gonadotropic hormone that are excreted. The author concludes that animal experiments with retained placentæ and observations on human beings point to the placenta's having an endocrine function in controlling gestation. There is an abundance of data on the profound changes that take place during pregnancy; but the unifying conception, which would make everything fall into place, remains elusive. The author's search of the literature leads him to suggest that the pregnant animal must be treated as a different animal, and that an entirely new start must be made in determining hormonic relationships. He also suggests that this may hold true for other physiological processes.

BIOLOGICAL CHEMISTRY.

The Blood Sugar Level in Relation to Hunger.

W. W. SCOTT, C. C. SCOTT AND A. B. LUCKHARDT (*The American Journal of Physiology*, July, 1938) have made blood sugar determinations on human subjects before, during and after normal "hunger periods" by the microchemical method of Miller and van Slyke. Within the range of experimental error (± 5·0 milligrammes per 100 cubic millimetres) no variations in the blood sugar level were found during the entire period. The authors conclude that the level of the blood sugar bears no causal relation to the normal "hunger periods" of man.

Renal Excretion of Electrolytes.

GEORGE W. THORN, LEWIS L. ENGEL AND HARRY EISENBERG (*The Journal of Experimental Medicine*, August, 1938) have studied the effect of the administration of suprarenal cortical extracts and crystalline compounds derived from the suprarenal cortex on the renal excretion of electrolytes. Of the compounds studied, all those which were effective in maintaining dogs from which the suprarenals had been removed were shown to produce a reduction in sodium excretion and chloride excretion and an increase in potassium excretion when injected into normal dogs. A crystalline synthetic compound, desoxy-corticosterone acetate, was successfully substituted for cortical extract in a dog from which the suprarenals had been removed, and produced in a normal dog a retention of sodium and of chloride and a potassium diuresis.

Lead Content of Human Blood.

CARL E. WILLOUGHBY AND ELWOOD S. WILKINS, JUNIOR (*The Journal of Biological Chemistry*, August, 1938), have estimated the lead content of the blood of 189 individuals, who gave no history of previous undue exposure to lead and who exhibited no symptoms of lead poisoning. Values were found ranging from zero to 0·09 milligramme of lead per 100 grammes of blood, with a most probable value of 0·025 ± 0·002 milligramme per 100 grammes of blood. In 58 samples serum was separated from cells and fibrin. Approximately 90% of these serum fractions contained no detectable amount of lead and only insignificant quantities of lead were found in the remainder. Although the most probable concentration of lead in the blood was considerably less than 0·09 milligramme per 100 grammes of blood, it was concluded that values of this magnitude might occasionally occur without indisputable clinical evidence of plumbism.

Estimation of Serum Protein.

BENJAMIN M. KAGAN (*The Journal of Clinical Investigation*, July, 1938) has described a simple, easy and rapid method for the determination of specific gravity by the use of the falling drop method. The materials and methods are described in detail. This method has been applied to the estimation of the total protein present in serum and in plasma, and is based on the linear relationship that exists between specific gravity and protein content. It provides a way of estimating the protein content of serum and plasma with an accuracy greater than that required for clinical purposes. The author states that it is about twice as accurate as the refractometric method. It has the advantage that extremely small quantities of blood can be used.

Normal Plasma Phosphatase Values.

A. S. MOLAY AND SAMUEL HORWITZ (*The Journal of Laboratory and Clinical Medicine*, August, 1938) review the literature dealing with plasma phosphatase. They state that there are only a few reports dealing with normal blood phosphatase values and that these have been obtained from a relatively small number of persons. They record the results of plasma phosphatase determinations on persons who showed no evidence of any abnormal condition known to alter phosphatase values. These subjects were newly born infants, children, adolescents convalescent from acute illness, and inmates of the San Francisco Home for the Aged. The Jenner-Kay method of estimation was used. The basis of this, as of all other methods for estimating phosphatase activity, is the measuring of the phosphorus liberated as inorganic phosphate when the enzyme is allowed to act on a substrate under standard conditions. One Jenner-Kay unit represents the amount of enzyme that will liberate one milligramme of phosphorus as free phosphate from an excess of disodium-β-glycerophosphate at pH 8·8 in three hours when kept at a temperature of 37·5° C. The phosphatase content of a sample of plasma is defined as the number of milligrammes of phosphorus that would be liberated by 100 cubic centimetres of plasma under the above conditions. The authors found that in infants under one month of age the plasma phosphatase values ranged from 4·0 to 11·5 units, averaging 6·85 units. From one to fifteen years of age there was apparently an increase in plasma phosphatase values; they ranged from 5·0 to 14·0 units, with an approximate average of 9·0 units. After fifteen years of age there was a rather rapid decrease in the phosphatase activity of the plasma until the age of twenty-five years; after that period the values remained relatively the same. Beyond the age of fifty years, the authors found a wider fluctuation in phosphatase values, with a lower minimal level.

The Value of the Urea Clearance Test in Pregnancy.

DORIS B. BROWN (*The Journal of Obstetrics and Gynæcology of the British Empire*, October, 1938) has attempted to assess the value of the urea clearance test in pregnancy, with special reference to the toxæmias of pregnancy. In all, 671 tests were carried out on 243 patients. The test was performed in the morning and only a light breakfast without tea or coffee was allowed before the test. The specimens of urine were all obtained by catheter, since it was found that many pregnant women, and more particularly many women in the puerperium, did not completely empty the bladder. In the case of the outpatients tested, a glass of water was given each hour to the patient to sip, as otherwise in many cases the volume of urine obtained was very small. The results obtained when this technique was established were remarkably constant. Both the urea content of the blood and the urea content of the urine were estimated by the urease method. This method of urinary analysis includes the preformed ammonia. Van Slyke finds that more consistent clearances are obtained from urea with ammonia than from urea alone. The author records the results of the use of the urea clearance test and discusses its interpretation in pregnant women. This interpretation frequently presents difficulties. The author observes that each case must be considered separately and on its own merits, and the clinical condition of the patient and the result of urea clearance tests must be judged together.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held in the Medical Society Hall, East Melbourne, on July 6, 1938, DR. J. P. MAJOR, the President, in the chair.

Diabetes Mellitus.

DR. EWEN DOWNIE read a paper entitled "Diabetes Mellitus (see page 975).

DR. J. R. BELL opened the discussion. We have not been able to obtain a report of his remarks.

DR. E. L. COOPER remarked at the outset that he wished to dissociate himself from Dr. Bell's remarks, which tended to depreciate the value of Houssay's attitude towards diabetes. Houssay and his fellow workers had carried out a tremendous amount of research in the field of metabolism, and Dr. Cooper believed that Houssay still considered *diabetes mellitus* to be due to disordered action of the pancreas and of the liver rather than of the pituitary gland. Houssay had stated that in all diabetes there was an insufficiency of insulin in relation to the needs of the organism, though the actual secretion of insulin might be normal or even increased.

Dr. Cooper said that slight under-nutrition based on a consideration of the total caloric value of the diet was advisable in all cases of *diabetes mellitus*. Strange diets, such as the molasses, paw-paw or prickly-pear diets, all meant under-nutrition of the subject. The correct treatment for adults was still under-nutrition; but the diabetic child should be fed in a satisfying manner, with the object of keeping him from breaking the dietetic regimen. With diets relatively rich in carbohydrate and moderately poor in fat, the carbohydrate tolerance often improved so long as the total caloric intake was kept low. Some diabetics did not progress even when receiving high caloric diets; but in general restriction of total caloric intake helped many patients to regain some degree of sugar tolerance. The advantage of a diet rich in carbohydrates was, as Dr. Downie had remarked, that it increased the efficiency of the available insulin, whether injected or self-produced. A high salt intake also increased the efficiency of insulin action. At present there was insufficient evidence as to whether Himsworth's conception of insulin kinase was correct; but the practical application of the idea was beyond doubt.

Dr. Cooper's only patients receiving diets rich in fat were those long-standing diabetics who had been on such a diet for so long a time that they had lost all liking for carbohydrates. They refused to take the newer diets, and he did not argue with them. Dr. Cooper said that he regarded the question of insulin sensitivity as a most interesting and important aspect of modern diabetic treatment. Many authorities divided their patients into those who were sensitive to insulin on the one hand, and those who were resistant to insulin on the other. Dr. Cooper said that it had long been known that one unit of insulin assisted the metabolism of different quantitative amounts of glucose in different individuals or in the same individual at different times. More recently, however, there had been a tendency to divide patients with *diabetes mellitus* into two groups. In the one group were the younger patients. They were sensitive to small doses of insulin and were apt to pass into hypoglycæmic coma; yet they showed no increase of sugar tolerance, even when the hyperglycæmia was efficiently controlled. Those patients were capable of dealing with a diet very rich in carbohydrates, and required little or no increase in insulin when the carbohydrate content was raised, so long as the total caloric content remained the same. The more carbohydrate that was given, the more sensitive was the patient to insulin. In the other group were the older diabetics who were relatively insensitive to insulin. In those patients the glycosuria was often discovered only on routine examination, and the diabetes was symptomless. The patients, in spite of the frequent association of hypertension and obesity, usually showed a progressive increase of tolerance to carbohydrate if the hyperglycæmia was carefully controlled. Although they were relatively insensitive to insulin the effectiveness of insulin increased with a diet high in carbohydrate, and might be assisted by means of liver extracts.

Dr. Cooper remarked that it was possible that the groups of diabetics he had contrasted represented the extremes in a scale of hyperglycæmias. At the one end were those due to purely pancreatic deficiencies; at the other end were the cases in which pancreatic secretion was normal in quantity, but its action was inhibited by extra-pancreatic factors, such as the pituitary secretions. It was only in childhood that total diabetes occurred. By that term Dr. Cooper meant the diabetes in which the patient apparently secreted no insulin at all and the glucose taken in was metabolized quantitatively by the insulin injected. Dr. Cooper explained that he had used the term "insulin resistance" in a sense different from that in which it was applied to those cases, fortunately rare, in which even enormous doses of insulin failed to reduce a high blood sugar level. He stated that he referred to the effect of infection, hyperthyreoidism and the strange changes that occurred at adolescence. The passage of a diabetic patient from childhood to adult life was often stormy. Larger and larger dosage of insulin was needed as the child increased in weight and height; but over and above the factor of body surface diabetes behaved in a peculiar fashion in children between the ages of twelve and fifteen years. Ketosis arose on the least provocation, coma was common, and often those children temporarily became resistant to large amounts of insulin. He went on to say that during ketosis arising after infections, particularly of the skin or renal tract, the children under discussion might show no response even to as much as 500 units of insulin a day, even when the insulin was given intravenously. It was necessary to mention the route of injection, because insulin injected subcutaneously might not be absorbed during the circulatory depression of extreme coma. Dr. Cooper also observed that the general statement could be made that less insulin was required for a patient at a time of increased physical activity, and that patients could readily learn the wisdom of reducing the amount of insulin injected subcutaneously just before a physical effort, such as strenuous participation in a game or race. He put forward the view that the insulin resistance at puberty and during adolescence was in some way due to the imbalance of the ductless gland secretions. It was known that sugar metabolism and insulin sensitivity were largely controlled by the pituitary, thyreoid and suprarenal glands. Those glands were all disturbed by the gonadal changes, and the temporary difficulties in the control of diabetic children might well be associated with the polyglandular dysfunction.

Dr. Cooper passed on from the question of diabetes in childhood to that of heredity in diabetes. He said that it was well known that in certain families diabetes was common. He had been struck with the frequency with which diabetes occurred in cousins, aunts and uncles, rather than in the parents of diabetics. That observation might be explained in part by the high fœtal mortality during pregnancy in diabetic women; this meant that relatively few children were born to diabetic parents. Although direct inheritance unquestionably occurred, and although approximately 25% of diabetics gave a family history of the disease, it had been Dr. Cooper's experience that collaterals were more often diabetic than were the parents or grandparents. In other words, diabetes was more often familial than hereditary. He commented on the enormous difficulties encountered in any attempt to construct an accurate family tree for a diabetic. Many people passed through life with undiagnosed diabetes. Many cases were discovered late in life; and often the children were unaware of the occurrence of diabetes in the parent. Diabetes was transmitted along Mendelian lines as a recessive characteristic, and a carrier might transmit the chromosome without developing the disease himself. Dr. Cooper pointed out that it was only the tendency to the

disease that was transmitted. The determining factors were many, and the susceptible individual might escape the disease if he did not meet with the requisite stress. Traumata, infections, nervous strain, obesity, a diet rich in fat, and disorders of the ductless glands, such as toxic goitre, were some of the known stresses that might produce *diabetes mellitus* in a suitable subject.

Dr. Cooper did not consider that diabetic subjects should be advised against marriage or child-bearing, though it could be pointed out to them that the diabetic mother was exposed to dangers during pregnancy and that difficulties might occur in the management of the children of the marriage. As the risk of inheritance was multiplied, it was extremely unwise for two persons with diabetes to marry. A history of tuberculosis in the family of a diabetic was an additional factor that should influence the decision not to marry, for diabetes complicated by tuberculosis was a much more serious condition than was either disease by itself.

Dr. Cooper stressed the necessity for carrying out estimations of sugar tolerance under standard conditions. He pointed out that the sugar tolerance curve might be upset if the patient had hurried to keep the appointment, or had spent a sleepless or restless night worrying about the outcome of the examination. In conclusion, Dr. Cooper expressed his appreciation of Dr. Downie's paper, and said that it represented not only a great deal of work, but also the fruits of a very wide experience in the treatment of *diabetes mellitus*.

DR. C. W. ROSS said that he wished to speak briefly in confirmation of what Dr. Cooper had said about the way in which *diabetes mellitus* could be divided into groups. Dr. Ross believed that, with the future development of knowledge and closer analysis of case records, not two, but three or four distinct clinical entities, and three or four overlapping groups, would be differentiated. The process would be somewhat similar to the separation of the hæmochromatoses; one patient might be a frank diabetic, another a frank cirrhotic, or there might be any possible mixture. Dr. Ross also made reference to a point of practical importance in the management of diabetic patients. The occurrence of ketosis might possibly simulate an acute medical or surgical condition when pain or cramp was a feature. The pain should be recognized as a salt-deficiency pain and should be abolished in a few minutes by the administration of hypertonic saline solution by the intravenous route.

Dr. Downie, in reply, thanked those who had contributed to the discussion. He said that he agreed with what Dr. Bell had said concerning the use of insulin if doubt existed or difficulty arose in the stabilization of a patient. A remarkable improvement followed when the use of insulin was added to dietary restrictions; the weight of the patient could be raised thereby. The amount of carbohydrate available to the patient was purely a question of medicine. It was unbelievable that in ten years they would still be using a diet similar to that which prevailed at present. Dr. Downie added that he had clinical confirmation of the value of the diet rich in carbohydate advocated by Dr. Priscilla White, for children who could with advantage be given 200 or even 300 grammes of carbohydrate each day. Dr. Downie expressed the view that protamine zinc insulin marked a signpost in the advance towards a better preparation. Like other clinicians, he had encountered variable reactions to it. He viewed the preparation with peculiar suspicion, which almost amounted to loathing. He considered that the dosage should not be altered rapidly, and was glad that Dr. Bell had expressed a similar opinion. Joslin had said that it was not wise to teach an old dog new tricks. Patients who were used to using the original insulin with satisfaction should not be advised to change over to the protamine zinc insulin. During treatment with protamine zinc insulin some patients experienced peculiar feelings when approaching the hypoglycæmic state, at a stage when glycosuria was still present and the hypoglycæmia was uninfluenced by food or sugar. He knew of no explanation of the wretchedness those people suffered. Dr. Bell had asked for an opinion about the use of the new preparation in diabetic coma. Dr. Downie said that he himself had had no experience on the point; but he knew that Rabinowitch had said that if so much as 100 or 200 units of protamine zinc insulin were given a comparatively rapid decrease in the depth of the coma usually occurred.

With reference to the treatment of threatened gangrene, Dr. Downie considered that Allan's practice of the use of cold applications was unphysiological; it might prevent spread of infection, but the circulation was imperilled. Lewis had advised that the application of heat, even dry heat, to the extremity was to be avoided, as it created a demand for an increased blood supply which could not be supplied without damage from congestion. The effective treatment was to heat the rest of the body and to leave the extremity unheated. The deferring of surgical measures in gangrene resulted in weeks of pain for the patient. Elderly subjects, who could not be expected to handle crutches or manage artificial limbs, should not have an amputation performed without the most careful forethought. Dr. Downie had patients who had all their extremities and were able to walk about five years, seven years or even ten years after amputation for diabetic gangrene had been under consideration. It was easier to keep the leg on than to put it back again. Dr. Downie pointed out that, as the majority of people ate far too much, the diabetic, in comparison, should assuredly be underfed.

Dr. Cooper had made Dr. Downie wonder whether diabetic patients suffered progressively. Dr. Downie was of the opinion that diabetes in a patient under proper control was usually not progressive, though progression was apt to occur if the treatment was allowed to lapse. In the management of insulin-sensitive and insulin-resistant patients, Dr. Downie advised that the insulin requirement should be lowered by the withholding of all food and the administration of nothing but glucose for the time being. Suitable dietary and dosage of insulin could then be worked out slowly and carefully. Dr. Cooper thought that the term "total diabetes" had no established justification. As an illustration of the way in which the lapsing of treatment could be correlated with insulin resistance and apparent progress of the diabetic state, Dr. Downie quoted a case in which stabilization had been effected on 20 units of insulin a day. After breaking away from controlled treatment for six months the patient had needed 80 units a day before stabilization was again established. Another lapse from treatment for a slightly longer period had followed, and stabilization was not effected until 240 units of insulin were injected daily. After another lapse she had died in coma. Five hundred units of insulin had failed to control the diabetes. Dr. Downie said that he and Dr. Cooper were willing to support the doctrine of Dr. Priscilla White that insulin should be used in almost all instances of diabetes in childhood, from the commencement of treatment. Dr. Downie referred to the variability of the response of children under treatment at rest. He advocated that the hospital should be used as a boarding house, from which the child could be sent to school or could follow his normal activity. Stabilization in children should be established for everyday activities. If it was effected while they were inert in hospital they were very apt to lose the stabilization shortly after going home, because of the increased activity under home conditions. Diabetes in children should not be allowed to interfere with normal development. A boy who had been his patient from the age of sixteen years had become a flyweight boxer of note; and it was well known that such performances were not uncommon. In conclusion, Dr. Downie thanked Dr. Ross for the information about the value of the intravenous injection of saline solution in removing the pain of ketosis.

A MEETING of the New South Wales Branch of the British Medical Association was held on July 21, 1938, at the Women's Hospital, Crown Street, Sydney. The meeting took the form of a number of clinical demonstrations by members of the honorary staff. Part of this report appeared in the issue of December 3, 1938.

Intracranial Damage in the New-Born.

DR. S. HARRISON showed cinematograph films from six cases of intracranial damage in the new-born. In the first case damage had occurred to the base of the skull, with laceration of the *tentorium cerebelli* on both sides and rupture of the straight sinus and *vena magna Galeni*. On the left side there was a complete tear of the free margin of the tentorium. On the right side only the upper fibres were torn. The condition was incompatible with life.

The second case was that of a premature baby, whose birth weight was 1·8 kilograms (four pounds). Delivery had been difficult and had been by the breech. The baby had suffered from *asphyxia pallida* and profound shock. On the second day screaming attacks had occurred, with pronounced twitchings of the face and limbs. The temperature rose to 38·4° C. (101° F.). All signs had disappeared twenty-four hours later. One dose of 0·0027 gramme (one-twenty-fourth of a grain) of "Luminal Sodium" was given. The sucking power was good and there was no cyanosis. Recovery was delayed by hæmolytic anæmia of the new-born. Dr. Harrison remarked that the disorder suggested the leptomeningeal type of intracranial hæmorrhage.

Dr. Harrison's third film related to a full-term baby, whose birth weight was 3·7 kilograms (eight pounds four ounces). Labour had been easy and normal. The child had never breathed, but heart sounds had been perceptible. Life had been maintained for ten hours by means of carbon dioxide and oxygen given from separate cylinders connected by tubing to a sphygmomanometer bag and thence to a tracheal catheter. The bag was rhythmically compressed manually. A blow-off valve set at a maximum of 12 millimetres of mercury was necessary to prevent lung damage. At autopsy petechial intracerebral hæmorrhages and intense surface congestion had been found.

The next film shown by Dr. Harrison related to a full-term baby, whose birth weight had been 3·5 kilograms (seven pounds twelve ounces). Labour had been easy, but had been complicated by the fact that the cord tightly encircled the fœtal neck. *Asphyxia pallida* had been present. The child had been restless and inclined to twitch on the first day. On the second day the temperature had risen to 38·9° C. (102° F.), subsiding in three days. Pronounced head retraction, pleurothotonos and tonic spasms had developed. The sucking reflex remained absent throughout the two months the child spent in hospital, nutrition being well maintained by means of tube feeding. The child was transferred to the Royal Alexandra Hospital for Children on April 14, 1938, in satisfactory general condition.

Dr. Harrison next showed films relating to a full-term baby, whose birth weight had been 3·1 kilograms (six pounds fifteen ounces). Labour had been normal. Twitching and hypertonus had appeared on the third day, accompanied by cyanosis and complete loss of sucking power, which had never been regained. The spasms gradually changed in type and became definitely clonic movements following on tonic contractions. Death occurred in forty-five days. At autopsy the brain was found to be intensely congested, but no macroscopic hæmorrhage was present. A hæmorrhage had occurred in the apex of the right lung.

Dr. Harrison finally showed films relating to a full-term baby, whose birth weight had been 3·9 kilograms (eight pounds eleven ounces). A forceps delivery had been necessary, and a depressed fracture of the left frontal bone had occurred. On the first and second days the child's condition had been normal. On the third day head retraction had developed. No twitchings were present. The colour and sucking power remained good throughout. The head retraction had disappeared in eighteen days and the baby had been discharged, well, nine days later.

Dr. Harrison said that intracranial damage might be subdivided into several types. The first of these was subdural hæmorrhage, chiefly tentorial tears. The second type was leptomeningeal hæmorrhage, which most commonly occurred in premature babies. The third type was intraventricular hæmorrhage, which most commonly occurred in premature babies and was always fatal. The fourth type of damage was intracerebral microscopic and macroscopic hæmorrhages.

Hans Heidler, in the *Wiener klinische Wochenschrift* for June, 1935, quoted in the 1935 issue of the *Year Book of Pediatrics*, at page 41, stated that 65% of infants born at term and 95% of premature babies had intracerebral hæmorrhages, often only microscopic in appearance, but that this type of bleeding was of more theoretical than practical interest. The grosser types, exemplified in the third of Dr. Harrison's cases, could cause death. The fifth type of intracerebral damage consisted of injuries not demonstrable anatomically. At autopsy meningeal œdema and hyperæmia might be the only findings. This group was not small.

Dr. Harrison went on to say that in three of the six cases delivery had been easy. Intracranial damage, therefore, was not necessarily associated with disproportion, with protracted or precipitate labour or with forceps delivery. It even occurred in Cæsarean section. The patients chosen for film presentation had displayed the more pronounced signs of intracranial damage; but it had to be remembered that the slightest transient optic and facial twitchings were enough to suggest the condition. Bulging of the fontanelle was comparatively rarely seen. In all these cases the mother's blood serum failed to react to the Wassermann test.

Abdominal Palpation in Pregnancy.

DR. T. DIXON HUGHES, in conjunction with DR. M. T. DRUMMOND, showed a film made at the Women's Hospital, illustrating abdominal palpation in pregnancy. The first part depicted the various types of abdomen, such as those in which twins or hydramnios were present, pendulous abdomen and oblique position of the fœtus. A good example of lordosis was noted, especially when the patient turned round. The part of the film depicting the palpation of the abdomen was gradually merged into another part depicting the palpation of a fœtus outside the abdomen, in the position it occupied in the uterus. By this means the portrayal of the actual palpation was made clearer.

Dr. Dixon Hughes also showed some X ray films to illustrate briefly the method of X ray pelvimetry according to Ball's technique. Dr. Dixon Hughes said that this method was one in which the fœtal head was expressed as a volume in cubic centimetres, and the smallest diameter of the pelvis was likewise expressed as a volume. It was stated that when there was a difference of more than 150 cubic centimetres excessive moulding would have to take place and cerebral damage would result. Dr. Dixon Hughes expressed the opinion that this could not be taken as definite at present, and that more work would have to be done before the exact value of this technique could be estimated.

General Peritonitis following Abortion.

DR. J. N. CHESTERMAN showed a patient who had been admitted to hospital after attempted illegal abortion by means of a catheter six days before. She had had amenorrhœa for three and a half months. Two days after the introduction of the catheter severe abdominal pains had developed. She had removed the catheter and had continued vaginal douching, but no miscarriage had occurred. On admission to hospital her temperature had been 38° C. (100·4° F.) and her pulse rate 120 beats per minute. She had had an anxious expression and had been in obvious pain. Her tongue had been dry and coated. On examination her abdomen was found to be generally distended, tympanitic on percussion and tender in all areas on palpation. An enlarged, tender uterus was palpable in the lower part of the abdomen. Examination *per vaginam* revealed pronounced tenderness in all fornices and a profuse mucopurulent discharge. On the following day her condition appeared worse, her temperature rising to 38·7° C. (101·6° F.) and her pulse rate to 136 beats per minute. The distension and tenderness of the abdomen were more pronounced. During the day she expelled a

fœtus developed to three months. Cultures from a cervical swabbing taken the previous day resulted in growths of the following organisms: aerobically, Gram-negative coliform bacilli resembling *Bacillus pyocyaneus*, which did not ferment lactose and grew in greenish colonies; anaerobically, large Gram-positive bacilli resembling the *Bacillus welchii*, some streptococci forming short chains, and other unidentified organisms.

A blood count revealed 4,550,000 erythrocytes per cubic millimetre. The hæmoglobin value was 80%. The total leucocytes numbered 23,400 per cubic millimetre, 89% of which were neutrophile cells.

The patient was given 20,000 units of gas-gangrene antiserum subcutaneously. On the following day there was no improvement. Her pulse rate remained at about 130 beats per minute, and the temperature at about 37·8° C. (100° F.). Severe abdominal pain and tenderness were present, and in addition some diarrhœa and vomiting. The patient was taken to the operating theatre and nitrous oxide and oxygen were administered. The uterus was explored with ovum forceps and some placental débris was removed. Posterior colpotomy was then performed and a large quantity of turbid fluid escaped. A large rubber drainage tube was then inserted and stitched into position. A small incision, 5·0 centimetres (two inches) long, was then made in the abdomen, in the mid-line above the *symphysis pubis*, and much seropurulent fluid escaped. The whole peritoneal cavity was found to contain seropurulent fluid. The omentum was œdematous and the peritoneum injected, there being no apparent attempt at localization by adhesions. The paracolic gutter was drained by rubber tubes through a stab wound in each side, and the pouch of Douglas was drained similarly, through the mid-line incision. When the patient was returned to the ward the intravenous administration of 5% glucose in normal saline solution was commenced by means of a slow continuous drip. This was continued for the following four days. On the day after operation the patient's general condition seemed slightly improved, although her pulse rate remained rapid, being between 120 and 130 beats per minute. A little vomiting occurred and there was a copious discharge from the drainage tubes. During the next two days there was a gradual improvement, manifested by lessening abdominal distension and a fall in pulse rate. The drainage tubes were turned and shortened and all removed four days after the operation. Cultures were made from the fluid from the abdominal cavity, Gram-negative coliform bacilli resembling the *Bacillus pyocyaneus* being grown. During the next few days the patient's temperature and pulse rate commenced to rise again, and as there was very little drainage from the colpotomy incision it was decided to reopen it. This was done on the eighth day after the first operation, the patient being under nitrous oxide and oxygen anæsthesia. Some dark-coloured pus escaped. A gauze strip was packed into the pouch of Douglas; this was gradually removed by being shortened a little each day. Although the patient's condition had improved, her temperature and pulse rate remained elevated without showing any tendency to subside to the normal. A second blood count revealed definite anæmia, the erythrocytes having fallen to 2,560,000 per cubic millimetre and the hæmoglobin value being 40%. The total leucocytes numbered 21,500 per cubic millimetre. A blood transfusion of 450 cubic centimetres of citrated blood was given. After this the patient showed steady improvement and was discharged from the hospital, well, thirty-nine days after admission. Dr. Chesterman said that he had examined this patient *per vaginam* about three months later, and had been able to find no gross abnormality in the pelvis or abdomen.

Dr. Chesterman's next patient was another young woman who had developed peritonitis after an abortion brought on by "syringing". She had miscarried a week previous to admission to hospital, and the miscarriage had been followed by severe pain over the whole abdomen. She had had vomiting and diarrhœa since the previous day. On admission she was gravely ill, with a temperature of 38·8° C. (101·8° F.) and a pulse rate of 130 beats per minute. Her tongue was dry and red. Her abdomen was moderately distended and did not move with respiration. On palpation generalized tenderness and some muscle guarding were observed. On percussion there was dulness in both flanks. Examination *per vaginam* revealed tenderness, but no bulging, in all fornices, and a brownish, purulent discharge from the external os. On the following day the patient's condition was slightly worse, her temperature reaching 39·3° C. (102·8° F.) and her pulse rate being continuously over 130 beats per minute. She had ceased vomiting, but her abdomen was more distended and still tender in all areas on pressure. Under nitrous oxide and oxygen anæsthesia a posterior colpotomy was performed and a very large quantity of thin, foul-smelling pus was evacuated. Because of the large quantity of fluid that was drained in this way it was decided not to open the abdominal cavity above the *symphysis pubis*. A long strip of iodoform gauze was packed into the pouch of Douglas through the opening in the posterior fornix, and this was shortened a little each day. It was finally removed at the end of one week. A culture was made from some of the purulent fluid, and it was found to contain Gram-negative coliform bacilli, *Bacillus welchii* and anaerobic streptococci. No organisms were grown on attempted culture from the blood. A blood count made at this stage revealed no undue anæmia; the erythrocytes numbered 4,150,000 per cubic millimetre, the hæmoglobin value was 65%, and the leucocytes numbered 30,000 per cubic millimetre. The day after operation the patient was still very ill, with vomiting and diarrhœa. Nevertheless there was less tenderness in the upper part of the abdomen, and her pulse rate on occasion subsided to less than 120 beats per minute. An intravenous injection of 10% glucose in saline solution was given. The next day the patient showed evidence of slight improvement, which was maintained till the day following; at that stage, however, she became slightly jaundiced in the skin and conjunctivæ. The erythrocyte count had dropped to 3,600,000 per cubic millimetre, the hæmoglobin value was 50%, and the leucocytes numbered 13,000 per cubic millimetre. The patient was given 40,000 units of gas-gangrene antiserum, and a similar dose was administered the following day. The icterus deepened during the next few days, although there was improvement in her general condition and the colpotomy wound was still draining freely. A blood transfusion of 350 cubic centimetres was given. The patient now complained of pain in the right iliac region extending out into the right flank, and during the next three days a tender mass developed in this region. She was again anæsthetized with nitrous oxide and oxygen and the mass was explored with a needle. Pus was found, and an abscess cavity deep to the musculature of the abdominal wall and lateral to the cæcum was drained by two incisions; a rubber tube was stitched in position in each. At the same time the colpotomy wound was reopened and pus was liberated. A further 10,000 units of gas-gangrene antiserum were injected subcutaneously. The patient was still febrile, her temperature varying between 38·4° C. and 38·9° C. (101° F. and 102° F.), and her pulse rate was correspondingly high. A blood count indicated that considerable blood destruction was still in progress; the erythrocytes now numbered 2,400,000, and the hæmoglobin value was 38%. A second blood transfusion of 450 cubic centimetres was given, and the patient reacted with a rigor shortly afterwards. The patient now slowly improved, the amount of pus draining from the abdominal and colpotomy incisions gradually lessening. A further complication occurred, namely, thrombophlebitis of the great saphenous vein in the left leg. This caused pain and pyrexia for a few days. Recovery from then on was slow but steady; she was discharged from the hospital, well, fifty days after admission.

Dr. Chesterman said that he had brought these two patients before the meeting for the purpose of stressing four points in the diagnosis and treatment of general peritonitis after abortion or child-birth. The first was the difficulty in diagnosis, since this type of peritonitis frequently caused few, or even none, of the usual clinical signs of peritonitis. He had found distension of the abdomen, tenderness on firm pressure and diarrhœa a valuable diagnostic triad. The second point was the need for early drainage of the peritoneal cavity. Even if

turbid fluid was not found, Dr. Chesterman did not consider that posterior colpotomy, or a small suprapubic incision, which need not be longer than 5·0 centimetres (two inches) and could be made under local anæsthesia, could harm the patient. Where turbid fluid was encountered free drainage should be established. He had seen several patients with generalizing peritonitis for whom drainage of the peritoneal cavity had not been undertaken. The results were invariably fatal. The third point was the value of the administration of glucose and saline solution by the continuous intravenous drip method, to replace fluid loss, to dilute toxins and to assist in maintaining nutrition. The fourth point was the need for bacteriological diagnosis of the organism causing the infection, so that the appropriate method of countering its effects could be adopted.

A History of Previous Difficult Labour.

DR. H. A. MCCREDIE showed several patients to illustrate one of the problems met with in antenatal clinics, namely, that of the multiparous gravid woman who gave a history of difficult labour. He said that for adequate treatment these patients required a full general examination, the taking of a detailed obstetric history and a careful observation of the uterus, pelvis and fœtus. The obstetric history was often difficult to obtain from the patient, and was seldom so detailed as was desirable. It was, however, very valuable in the elucidation of the cause of previous dystocia. Dr. McCredie said that the information to be sought included: (i) the date of the previous labour, (ii) the stage of gestation, (iii) the weight of the child, (iv) the total number of hours in labour, (v) the number of hours in the second stage of labour, if ascertainable, (vi) the presentation and position of the fœtus, and (vii) the manipulations performed.

Dr. McCredie said that the examination of such patients should include the usual abdominal inspection, palpation and auscultation, mensuration of the pelvis and uterus, and a vaginal examination. The earlier in pregnancy the vaginal examination could be made, the better; some uterine and ovarian tumours could be dealt with surgically in the early months. The history and examination might reveal causes of dystocia that might reasonably be expected not to recur, such as hydramnios and hydrocephalus. Other causes might be found that could be rectified during the antenatal period, such as abdominal tumours or malpresentations and malpositions of the fœtus. Yet other causes of difficult labour, such as some organic rigidity of the tissues or contracture of the bony pelvis, would still be present in subsequent labours. Dr. McCredie remarked that some women would always produce a fœtus of excessive size, and these presented problems in disproportion. Any apparent disproportion focused attention upon the size of the fœtus. Some idea of this might be gained by examination of the patient at more frequent intervals after the thirty-fourth week, and by estimation of the size of the fœtus by palpation and mensuration. Dr. McCredie then gave the obstetric history of a patient that illustrated the importance in the problem of the variable factor of fœtal weight. The patient was a *multipara*, aged twenty-seven years. In 1932, after a gestation of forty weeks, she was delivered of a stillborn infant, weighing 4·3 kilograms (nine and a half pounds). Labour was difficult, and instruments were used. In 1933, after a gestation of forty weeks, she was easily delivered of a child weighing 2·7 kilograms (six pounds). In 1936, after a gestation of forty weeks, she was delivered of a stillborn infant weighing 5·2 kilograms (eleven and a half pounds). Labour was complicated by a breech presentation and was followed by the death of the mother.

Dr. McCredie said that more use could be made of radiography in determination of the degree of disproportion. A watchful eye was always kept on *primiparæ*; but a strong case could be made out for increased solicitude about *multiparæ*. During the preceding twelve months, out of the 56 Cæsarean sections performed for all causes at the Women's Hospital, 13 were for disproportion in *multiparæ*. The *multipara* with a bad obstetric history and a relatively large fœtus was best regarded as a candidate for trial labour. She should be admitted to hospital before term, so that a Cæsarean section could be undertaken if necessary.

The first patient shown by Dr. McCredie was a *multipara*, aged twenty-three years. Thirteen months previously, after a difficult labour, she had been delivered of her first child, which was stillborn. When she next presented herself examination revealed no pelvic abnormality. The abdomen was enlarged to the size of a three-months pregnancy, and a cystic mass, about 6·25 centimetres (two and a half inches) in diameter, was present in the posterior fornix. The patient was admitted to hospital. Operation was performed on March 24, 1938, and a dermoid cyst of the right ovary was removed. Dr. McCredie said that at the time of the meeting the pregnancy was still progressing. The patient had been discharged on April 14 to attend the out-patient department for further observation.

Dr. McCredie's second patient was a *multipara*, aged twenty-four years. She had had one child, weighing 5·4 kilograms (twelve pounds) at birth three and a half years earlier. Manual removal of the retained placenta had been necessary, and she had had to have a blood transfusion. The perineum had not healed completely, an elevation of temperature had persisted for several weeks, and her stay in hospital had been prolonged.

Examination revealed a pregnancy of about thirty-seven weeks' duration. The pelvic measurements were: interspinous, 25·0 centimetres (ten inches); intercristal, 30·1 centimetres (twelve and a half inches); external conjugate, 23·1 centimetres (nine and a quarter inches). The patient weighed 111·1 kilograms (seventeen and a half stone). The uterus was much enlarged and the amount of *liquor amnii* was small. The fœtus was presenting by the vertex and was in the right occipito-anterior position. The fœtal heart sounds were present, and there was no engagement of the head at the brim. The fœtus was regarded as being of excessive size, and the patient was recommended for admission to hospital.

Dr. McCredie's third patient was a *multipara*, aged forty-two years. She had first presented herself at the hospital in 1935. At that time she said that she had had two previous difficult labours, the children being stillborn. The first child had weighed 5·0 kilograms (eleven pounds) and the second 5·9 kilograms (thirteen pounds). The pelvic measurements were not abnormal and the patient's blood serum did not react to the Wassermann test. She was then pregnant with a fœtus of excessive size and was admitted to hospital. She was delivered by Cæsarean section of a living child weighing 4·5 kilograms (ten pounds). Dr. McCredie said that she had recently been discharged from hospital after a second Cæsarean section, by which she had been delivered of a child weighing 4·7 kilograms (ten and a half pounds).

Some Cardiac Abnormalities in the Newly Born.

DR. E. B. DURIE observed that congenital heart disease appeared to be one of the least common causes of neonatal death. Since January, 1931, 345 autopsies on stillborn or newly born infants had been performed at the Women's Hospital. In only 14 of these were congenital defects of the heart found, and in only 10 of these cases was death due to the presence of the cardiac abnormality. Some of the infants in this series had survived for a few hours, some for a few days. There was no record of the finding of a congenital malformation of the heart in a stillborn child. Approximately 21,000 infants had been born in the hospital during this time, with 532 neonatal deaths, so that the percentage of neonatal deaths proved to be due to congenital heart disease was about 0·2. These figures were incomplete, because the number of autopsies was considerably less than the number of deaths; but they suggested that congenital heart disease was a somewhat rare cause of death in the neonatal period and that the death of a newly born child should not be attributed to congenital heart disease unless an autopsy had shown this defect to be present. The majority of infants with congenital cardiac abnormalities survived the neonatal period, though many died during the first year of life. It

was only the grosser cardiac defects that caused death in the newly born; these were usually abnormalities which could not be adapted to the sudden changes that took place in the fœtal circulation at birth. As to the nature of the congenital malformations found, in four cases aortic atresia was present, in two there was pulmonary atresia, and in one of these a septal defect was also present. One case each of mitral atresia with defect of the interventricular septum and of tricuspid atresia was recorded. Of the two remaining subjects, in one defects of the interauricular and interventricular septum were present, and in the other the interauricular septum was absent. Eight of the ten infants were male and two were female. It was a curious fact that, according to writers on this subject, the most pronounced developmental defects almost invariably occurred in male infants, whereas the slighter defects were more common in females.

Dr. Durie showed lantern slides made from photographs of three specimens exhibited. The first was that of the heart of a female infant which had lived for three days. There was complete absence of the interauricular septum with dilatation of the right auricle and ventricle. The second slide was of a vertical section of a heart in which aortic atresia was present. There was no communication between the small, thin-walled aorta and the very small atresic left ventricle. The mitral cusps were small and deformed; the left auricle was extremely small. The right auricle and ventricle were dilated. The child, a male, had survived for three days. Two photographs of a third specimen were shown; in this there was pulmonary atresia, with a very pronounced defect of the interventricular septum, which was represented by a thickened band. The *foramen ovale* was widely patent. This resembled the combination of defects known as the tetralogy of Fallot, except that the aorta was not dextroposed. In this case the child, a female, had lived for four days. In these two cases the heart at autopsy had been surrounded by blood clot and recently formed adhesions. Rupture of the heart had taken place before death.

Dr. Durie remarked that nothing was known of the forces that disturbed the normal development of the fœtal heart. The critical period of development was from the fifth to the eighth week of intrauterine life, during which time the septa were forming, the *bulbus cordis* was undergoing involution, and torsion of the great vessels was taking place. De Zalka, quoted by Maude Abbott, had attributed some cases of pulmonary stenosis with closed septum, or aortic stenosis with closed septum, to late fœtal myocarditis or endocarditis, with resultant scarring in the conus wall below the valves. The fact that other congenital malformations so often accompanied pulmonary or aortic atresia made it almost certain that these conditions were due to developmental errors and not to fœtal myocarditis.

NOMINATIONS AND ELECTIONS.

THE undermentioned have been elected members of the Victorian Branch of the British Medical Association:

Ferris, Allan Aveling, M.B., B.S., 1936 (Univ. Melbourne), Ulverstone, Tasmania.

Mabin, Francis Robert Turnbull, M.B., B.S., 1935 (Univ. Melbourne), 132, North Road, Brighton, S.5.

Rochlin, Oscar, L.M.S.S.A. (London), 1938, 157, Spring Street, Melbourne, C.1.

Proceedings of the Royal Commission Appointed to Inquire into Matters Pertaining to National Health Insurance.

Monday, November 28, 1938.

Mr. Weston: Gentlemen, before evidence is called, there is a matter I desire to mention. I wish to refer to the document appearing at page 28 of Mr. Brigden's printed evidence. In that, it is stated that the representatives of the Federal Council said that the present rates in Victoria had been accepted by the profession under duress. While not suggesting for a moment any lack of good faith, I am instructed to state that those rates were not imposed by any duress, and I am also instructed to express regret that any contrary impression was created. I also wish to guard against this statement being taken as any admission that the Victorian rates have been adequate at any time material to this inquiry.

Mr. Dovey: If the Commission pleases, in view of my learned friend's statement just made, it seems to me that one of the reasons which actuated us in having a number of medical witnesses called from Victoria at this stage of the enquiry no longer exists. . . .

The Chairman: My own feeling—I am only speaking for myself at the moment—is that it is certainly quite unnecessary to call any medical men in order to further elucidate the position as to the relations between the lodges and medical men in Victoria and the rates that have been arrived at. There is no need to call evidence upon that aspect of this inquiry. Then comes the question as to whether it is necessary to bother busy professional men to come here to give evidence upon any other matter. . . .

Dr. Mulvey: I would like to know what Mr. Weston's view is, not as to accepting the rates under duress, but as to the adequacy or otherwise of the lodge rates in Victoria as compared with the rest of the Commonwealth.

The Chairman: Let there be no misunderstanding about this. Mr. Weston, as I understand, this morning clearly indicated that he in no way admits that the prevailing lodge rates or any past lodge rates have been adequate.

Mr. Weston: That is to say, at any time relevant to the inquiry.

The Chairman: Exactly. That is the way you guard yourself expressly upon the point.

Mr. Slater: The friendly societies, of course, contest the question of inadequacy.

The Chairman: Yes, that is in issue. It is going to be one of the matters to be fought out between the lodges and the British Medical Association. So that we may take it as quite clear that Mr. Weston at the present moment indicates that he will contend that the lodge rates in Victoria have never at any time been adequate.

Mr. Weston: Yes, Your Honour; and I think, Dr. Mulvey, that answers your question.

Mr. Slater: Of course Your Honour knows our position.

Chairman: Yes. You contend to the contrary.

Mr. Slater: As far as the question raised by Mr. Weston this morning is concerned, we appreciate that, but we say that that is answered completely, and we hope to dispose of the question.

Mr. Dovey: I only want to make the position perfectly clear to my friends. While I appreciate my friend Mr. Weston's attitude in not admitting anything in respect to adequacy of remuneration, I desire to say now that one argument that it seems to me would meet any such submission as my friend indicated he might make, would be propounded on the evidence given by almost every doctor called from Victoria so far, that when he went into practice he either bought or subsequently acquired a contract practice.

Chairman: That is quite so.

Mr. Weston: Need we argue it?

Chairman: I am not inviting any side to argue that matter.

Mr. Dovey: I was only seeking to say that it might be fairly assumed that if the witnesses who have not yet been called, but whom it was intended to call, are called, they would say substantially the same as those who have been heretofore called.

Chairman: I anticipate that they could say nothing else. At the very beginning of this inquiry I indicated that the test to be applied to rates of this kind, or the main test, is the market price. What has been the market price? In Victoria the market price has been 20s. and 25s. . . . It may be that the market price was influenced by the greater economic strength of the lodges, influenced down to a rather low level, or it may not be, but that was the current price just in the same way, generally speaking, as the wages of any other class of labour are fixed. The wages of all classes have remained the same until the institution over which I preside intervened, wages being subject to what Mr. Justice Higgins called "the haggling of the market". It is economic stress which has fixed these lodge rates just as the wages of other labourers have been fixed by economic stress, that is by competition. What are they prepared to do the work for? Hitherto they have been prepared to do it for 20s. and 25s. It may be that we will think it inadvisable to regard that as being adequate; that is a matter for further consideration after hearing the arguments of everyone.

Mr. Weston indicated that Dr. Embelton, who desired to give evidence to the Commission, would give evidence in Sydney when the sittings were resumed there.

Dr. Donald Dunbar Coutts, of Williamstown, was called as a witness by Mr. Dovey. Dr. Coutts gave confidential evidence concerning his contract and private practice and also described a private contract arrangement that he had with certain of his elderly patients.

Dr. Coutts also described certain panel practices that he had seen in Scotland and England; in cross-examination he explained that his experience of the practices he described was limited to visits of only a day's duration.

Dr. Lee Thornton Wedlick, of North Fitzroy, was called as a witness by Mr. Dovey. He gave confidential evidence concerning his contract and private practice. Dr. Wedlick described a panel practice that he had seen in the East End of London as "frightfully depressing".

Mr. Dovey: He had his price up outside?

A.: Yes.

Q.: Did you see any of the better class work?

A.: No, the only panel practice I saw was in the East End.

Q.: Would you agree that there are no conditions in Melbourne comparable to conditions in which that practice was carried on?

A.: No, the doctor was just a clerk.

Q.: But the conditions under which the people were living in that district were very much worse than anything you would see in Australia?

A.: Yes.

Dr. Edward Gregory Bannon, of Warrnambool, was examined by Mr. Bowie Wilson and gave confidential evidence concerning his practice.

Mr. Slater: If the Commission pleases, I desire to mention a matter that is one of personal convenience, because I understand from my learned friends that it looks as if the evidence here will be concluded tomorrow.

Chairman: Yes.

Mr. Slater: Then I understand that the Commission will resume in Sydney next Monday. What I am concerned about is when it is thought that final addresses might commence. As far as the Victorian and New South Wales friendly societies are concerned, Mr. Williams proposes to address the Commission on behalf of the friendly societies in New South Wales, and I propose to do the same in regard to the friendly societies in Victoria. We had at one stage contemplated the engagement of counsel for the joint task, but we have decided otherwise.

Chairman: Have you any suggestion to make as to the time of addresses, Mr. Weston?

Mr. Weston: I should think that the evidence would commence on Monday, and conclude during the week, and that the addresses might commence on the following Monday.

Chairman: That is in accordance with our own ideas of what will be convenient, so we will resume evidence in Sydney on the 5th, proceed with the evidence and finish it, and then the final addresses will be deferred till the following Monday, 12th December.

Dr. Alfred William Harley, of Thornbury, a residential suburb for industrial workers and clerical workers, was called as a witness by Mr. Dovey and gave confidential evidence.

Mr. Dovey: What is your experience of the amount of treatment that the wives of members require?

A.: When the husband comes he generally has some definite complaint that can be fairly easily elucidated and dealt with, but with the women and children their complaints are often more vague and take a good bit more time to sort out to ascertain whether it is a genuine case or not.

Q.: Do you think it would be fair to say that for every twice the man came to see you the woman would come at least three times?

A.: It depends; with women and children I would say yes.

Q.: Leave the children out; taking husband and wife, on the average do you say the wives would make at least half as many visits again as the husband?

A.: It is very hard to say that definitely. You see the wives more often, and they often bring the children with them, and it is hard to estimate.

Q.: I suppose in point of fact when there is a family you see the wife's name five times to the man's once?

A.: Yes. But it is quite often on account of the child that the wife brings along.

Q.: But you have not any impression one way or the other of alleged sickness experience of women as compared with men?

A.: I can say that they would consume more time in the aggregate than the men, but whether they make a greater number of visits would only be an impression, and I could not be sure.

Q.: Are they more disposed to ask for medicine than the men? Do they ask you to give them something for their trouble?

A.: I do not think any much more than the man; but the man does not like to go out of the surgery if he has a complaint, without some medicine, any more than a woman. I do not think the women return more often than the men.

Q.: Have you any views on the habits of contract patients coming back for a repetition of their mixtures? They have come along to you in the first place, and they have indicated to you that they have some trouble and they want a bottle of medicine. You have given it to them believing that it will do them good and possibly finish up the trouble; comparing the habits of men and women do you meet with any experience of their coming back unnecessarily for repetitions of such medicines?

A.: It is a bit more frequent in women. There is always a certain number, not a very big proportion, that come back very frequently, and seem to like taking the medicine, and they can always rake up some new additional symptom to emphasize the necessity for continuing it.

Q.: And I suppose in many cases if you know it will not do them any harm, and it may do them good, you decide that the best way out of the situation is to give them a repetition of the medicine?

A.: That is so.

Dr. Harley was cross-examined by Mr. Slater.

Mr. Slater: Your friendly societies practice has grown, has not it?

A.: Yes.

Q.: I suppose you have not resisted this growth? You have accepted all that have been willing to go on to the lists?

A.: I have accepted it as an established institution, and one which particularly applies to the district in which I work, and is therefore unavoidable.

Q.: You had, of course, the right and opportunity to refuse any accretion to your lists?

A.: Yes.

Q.: And I take it that you did not object, but you accepted the new members and did not regard them as calling for the passing of an examination?

A.: Yes.

Q.: Your relations with the friendly societies have been always cordial?

A.: Yes.

Q.: Have you taken any part in any movement for the variation of the medical agreement?

A.: In connexion with the friendly societies?

Q.: Yes.

A.: I have taken no active part.

Mr. Weston: I have no questions to ask.

Mr. Dovey: Are there any observations you would like to make in regard to any matter into which the Commission is inquiring? I do not want to shut you out from saying anything.

A.: I do not think I have at the moment.

Q.: You have watched our deliberations with some interest?

A.: Yes, I have endeavoured to follow the proceedings. No, I have nothing to add. I am here merely to answer questions. . . .

Dr. John Norval Burgess, of Brunswick, an industrial suburb, was examined by Mr. Dovey. Dr. Burgess gave evidence concerning his private practice and his appointments at the Friendly Societies' Brunswick and Coburg Dispensary and under the National Co-operative Company.

Mr. Dovey: What is your experience with respect to the number of visits you get from the husband compared with the wife. I mean how often does the wife visit you for each time the husband visits you?

A.: It is hard to estimate, but I should say, roughly, including wife and children, three to one. I have just tried to keep a check since I got the *questionnaire* on the ones who have come in during the last month, and it is estimated to be about three to one.

Q.: I suppose that, very often, when the wife comes for her treatment, the children come with her, and *vice versa*?

A.: Yes.

Q.: Leaving out the children, can you tell us your experience?

A.: I have not been able to check it this month, but I should say that it is about half and half for husband and wife. That is just an estimate.

Q.: You mean that you would see the husband just as often as the wife?

A.: Just about. That is for their own illnesses.

Q.: That is your idea, but you have not been able to check it?

A.: No; it is just an opinion.

The Commission, at 3.45 p.m., adjourned until the following day, Tuesday, November 29, 1938, at 10.30 a.m.

Tuesday, November 29, 1938.

Dr. Francis John Foley, of St. Kilda, was called by Mr. Dovey and gave confidential evidence concerning his contract and private practice.

Mr. Dovey: Do your lodge patients trouble you much with unnecessary calls?

A.: Some do, and some we never see.

Q.: Of whom do you see the most, the men or the women?

A.: I think the women.

Q.: Take an average lodge family, a man and wife, how often do you think you would see the wife on an average, compared with the man?

A.: I would see the wife three or four times at least to the man.

Q.: That is on her own account?

A.: Yes.

Q.: What other figures have you for us?

A.: That is about all I have.

Mr. Weston: I have no questions.

Dr. Francis George Travers Champion de Crespigny, of Ararat, which is about 127 miles north-west of Melbourne, was called by Mr. Dovey and examined by him as to confidential matters.

Mr. Dovey: What is your experience in Ararat as to the frequency with which you are called upon to attend to wives compared with the members?

A.: I see the wife and children very much more frequently than the man.

Q.: Leaving the children out of consideration for the moment, take the wives compared with the man?

A.: I should not think there is a great deal of difference.

Dr. William Herbert Ward, of Footscray, was called by Mr. Dovey and examined by him as to confidential matters. He was cross-examined by Mr. Slater.

Mr. Slater: Has your practice grown?

A.: Yes.

Q.: You have not refused any increases to your lists at all?

A.: No.

Q.: As a matter of fact, you agree that the work forms a very valuable part of your practice?

A.: Definitely.

Q.: I think that, with the capitation fees and what you told Mr. Dovey, as to an amount equivalent to about 60% of that figure, it accounts for almost half the gross proceeds of your practice?

A.: Yes. There is one observation I would like to make: Actually, when I came to Victoria from New South Wales and bought into this practice I had national health insurance in mind. That is thirteen years ago, and I figured that as the capitation fee was so low in Victoria, the increased value of the practice in Victoria would be very great when national health insurance came in.

Mr. Weston: It was an investment of capital in the practice?

A.: Yes, in that way.

Mr. Slater: During that period of time, have you taken any part in any movement for an increase in the capitation rates?

A.: I have not taken part in any movement, but on very frequent occasions I have exhorted at medical meetings that something should be done.

The Chairman: You have always supported the resolution?

A.: Definitely, yes.

Mr. Slater: Where has the resolution stayed? It has apparently stayed within the confines of the B.M.A.?

A.: I would hate to criticize.

Q.: Would you be surprised to know that none of those resolutions has yet been conveyed to the friendly societies' organization?

A.: No, I am not surprised, but at the time when that movement was gaining great ground, I am quite certain that if it had not been for the depression those resolutions would have strongly come before friendly societies.

Q.: Quite a lot of things might have come, too, but for the depression. During the depression the friendly societies, you know, kept all their members good on the books, did they not?

A.: No, not all of them. We had a slight dropping off. They paid for a certain number, but not all of them.

Q.: Probably there were secessions, but the bulk of the members were kept on?

A.: Yes, they were.

Dr. Harley Grover, of Port Melbourne, was called by Mr. Dovey and gave confidential evidence.

Mr. Dovey: Can you tell us how many services you gave to the patients?

A.: No, it is quite impossible; I cannot tell you that. I only keep a financial record of them.

Q.: What is your idea of the frequency with which the wife comes along to see you, compared with the husband?

A.: It is much more frequent.

Mr. Weston: By herself?

A.: By herself or with her children.

Mr. Dovey: I want to exclude children for the moment. In your practice what is the sickness experience, or alleged sickness experience of the wife as compared with the husband?

A.: I should say it is from 2 to 2·5 to 1.

Q.: Having in mind the number of services you give, it seems you are fairly well paid for your services to private patients?

A.: I think we are in an industrial suburb. A colleague of mine moved from Port Melbourne to Toorak and he told me it was the worst move he ever made. That was from a financial aspect. It is a saying in Port Melbourne that if you are not paid within three months you will not be paid at all. He told me that in Toorak he was rarely paid under twelve months.

Mr. Weston: I have heard the same thing about Darling Point.

Witness: He told me that in all seriousness.

Mr. Slater: Your contract practice has grown considerably?

A.: Yes.

Q.: You have not resisted that growth?

A.: Not at all; I welcome it.

Q.: You want it?

A.: Yes.

Q.: You regard them as a very valuable part of your practice?

A.: Yes, I do.

Q.: Have you taken any part in any movement for the variation of the medical agreement with regard to rates?

A.: Only by attending the British Medical Association meetings, but nothing further. I have taken no active part.

Q.: But when the matter has been discussed and resolutions have been carried?

A.: Yes.

Q.: Has that been a matter of frequency at all?

A.: The different British Medical Association meetings have been held and I have attended them, but I cannot say how many there have been.

Q.: Do you regard it as an active movement?

A.: I have not taken a particularly active part.

Dr. Maxwell Hoban, of Maryborough, which is about 105 miles from Melbourne, was examined by Mr. Dovey as to confidential matters.

Dr. Hoban described the operation of a mill benefit society by means of which the female employees of the knitting mills secured medical and dental service for a payment of sixpence a week, which was deducted from their wages.

Dr. Roderick John Aitchison, of Brighton, was examined by Mr. Dovey as to confidential matters, then as follows:

Mr. Dovey: What is your attitude to lodge practice; you are prepared to take as many as come along, I suppose?

A.: Yes, up to a limit, which I have not reached.

Q.: But you have some 500 members now?

A.: Yes.

Q.: Have you any idea how many dependants they have?

A.: No, not the faintest.

Q.: That does not trouble you?

A.: I tried to find out, but I could not. I asked two or three of the lodge secretaries, and they told me they had not the slightest idea.

Q.: While we are on the question of dependants, I think you have been in court and you heard Dr. Hoban give some evidence about the frequency with which wives come to visit him compared with their husbands. What is your view on the matter?

A.: I do not think there is such a great discrepancy personally. I think that the wives come more often than the husbands, but not to any marked degree.

Q.: Dr. Hoban said that, in the case of the childless wife, she came to him half a dozen times to her husband's once. Let us take the average wife. How often do you think she would come compared with the husband? You say there is a discrepancy?

A.: Yes. We will say that, of 100 visits by the two sexes, somewhere round about 60% would be the wives.

Q.: Are there any other matters upon which you would care to make any observations now that you are here? You know the nature of the subject into which we are inquiring?

A.: As far as the lodge practice is concerned I think it is largely satisfactory, and quite a lot of the satisfaction is undoubtedly due to the indirect gains—pecuniary satisfaction which comes from indirect gain inasmuch as the friends of the lodge patients come to me as a private patient.

Dr. Daniel John Comyns Crotty, of East Camberwell, was called by Mr. Dovey and examined by him as to confidential matters.

Dr. John Edward Cockerell, of Abbotsford, was called by Mr. Dovey and examined by him as to confidential matters.

Mr. Dovey: I understand you have some views you desire to put before the Commission concerning consultation hours?

A.: Yes. It is in regard to what I have heard as to what I am expected to do under the national health insurance scheme, and I desire to state that I consider what they are asking me to do is completely impossible.

Q.: What do you regard as being impossible?

A.: I would like to state that in one year I had 10,780 visits to my surgery.

Dr. Cockerell then described the manner in which he counted attendances and, after dealing with visits away from his surgery continued: So, if I have got to do those, that means a total of 14,000, and then I have got to write out a report on each of those visits, and even write down the prescriptions that I have given; well, I say it is a complete impossibility.

Q.: I think you are under a misapprehension there, doctor, all that you are expected to do would be to make a tick on a card.

A.: I have listened to a few meetings that we have had.

Q.: Do not take any notice of what you have heard at meetings.

A.: I have not heard them contradicted yet.

Q.: Look at this card; this is the sort of card that you would have to tick on the corner column, such treatment as you thought the visit required, and in this column there is the diagnosis.

A.: Well, even that much I consider to be as bad. If I had to do that for a lodge member the number is only 1,100, but I heard it suggested that there were possibilities of some people having 2,500.

Q.: Do not forget in regard to the 1,100 that you have their dependants as well.

A.: Granted that; still, if I get my dependants and they work out at something like 2s. 6d., if I work those out it will not come to so much more.

Q.: In order to allay your fears, the only persons whom any insurance would concern would be the insuree, not the dependants. You do what you like in regard to any dependants.

A.: I am only dealing with 1,100 here. I am presuming that I would have to deal with 2,500. I want you to understand that I am in an industrial suburb where all my practice, which is reasonably considerable, will be swept away from me altogether.

Q.: That is to say all those insurable persons who are now private patients are likely to become insurees?

A.: I think they would, with very few exceptions. The only exceptions would be those that I got out of my private patients and people who are in business, all the others are employees. It is almost exclusively a factory area.

Q.: What is the trouble about the hours?

A.: It will mean that I will have to work longer, and I do not want to work any longer. I think that when I have had my hours curtailed by a number of my lodge patients keeping to the lodge agreement, which means that those calls are to be in before half past nine in the morning, I think that would be sufficient.

Q.: You feel that there should be some deterrent against your being called out from your surgery unnecessarily?

A.: Exactly.

Q.: Then you may take it that evidence has been given that arrangements will be made to prevent that?

A.: I am very pleased to hear it.

Dr. Cockerell withdrew. After some discussion of a general nature the Commission adjourned.

The Commission, at 1 p.m., adjourned until Monday, December 5, 1938, at the Bankruptcy Court, Commonwealth Buildings, Sydney, at 11.30 a.m.

Correspondence.

MEETING OF THE COUNCIL OF THE VICTORIAN BRANCH.

SIR: In a report of a meeting of the Council of the Victorian Branch of the British Medical Association in your issue of November 26, 1938, under the caption "Salaries of Medical Officers of Health", certain statements are attributed to Dr. Merrillees. I wish to state that my report to the Council was a verbal report of a verbal interview and the abbreviated record, as appearing in the minutes, does not convey the sense of what was intended. On reading the report it would appear that Dr. Merrillees's general statement was specifically applicable to Dr. Lincoln's position, but that is not so.

Dr. Merrillees's personal opinion was that a minimum rate of £50 is ill-advised in that in some cases it is overgenerous, in others it is inadequate; but it was not intended to associate that opinion with any salary which might be paid to Dr. Lincoln.

Yours, etc.,
C. H. DICKSON,
Medical Secretary.

Medical Society Hall,
426, Albert Street,
East Melbourne, C.2
November 28, 1938.

The Royal Australasian College of Physicians.

INAUGURAL MEETING.

IN connexion with the inaugural meeting and ceremonies of the Royal Australasian College of Physicians to be held at Sydney from Tuesday, December 13, to Saturday, December 17, 1938, we have been asked to publish the following additional information.

Registration.

Fellows and members are asked to register either at the office of the college, "Craignish", 185, Macquarie Street, Sydney, on Monday, December 12, or at the Robert H. Todd Assembly Hall, British Medical Association House, 135, Macquarie Street, Sydney, on Tuesday morning, December 13. On registration, invitation cards to all functions will be issued.

Wives and daughters are asked to accompany visiting fellows and members from New Zealand and other States when they register on Tuesday morning, December 13. The object of this is to make adequate arrangements for entertainments additional to the official functions.

Inaugural Ceremony.

The inaugural ceremony, to be held in the Great Hall of of the University of Sydney on the evening of Wednesday, December 14, 1938, will begin at 8.30 with the entry of His Excellency the Governor, the President and councillors. Fellows and members and their wives or daughters are asked to be seated by 8.15 p.m. A special section of the Great Hall has been reserved for them. A programme of organ music will be played from 8.15 p.m. to 8.30 p.m.

Late Afternoon Party.

The late afternoon party will be held in the banquet hall of the Hotel Australia, at 5 p.m., on Thursday, December 15, 1938. At this function visiting fellows and members with their wives or daughters will be entertained by their New South Wales colleagues. The fellows and members living in New South Wales are reminded that tickets at a cost of 7s. 6d. are available at the office of the college, 185, Macquarie Street, Sydney. The New South Wales fellows and members are also informed that they may invite as many additional guests (not necessarily associated with the college) as they desire. Admission will be by ticket only.

Garden Party.

The garden party will be held at 3.30 p.m. on Friday, December 16, 1938, at "Loch Maree", 1, Coolong Road, Vaucluse (the home of Mr. and Mrs. Arthur M. Eedy). The council hopes that this will be one of the most pleasant and successful of the functions of the college.

Special General Meeting.

As the special general meeting concerns an important alteration in the constitution, fellows are reminded that their attendance is requested at this meeting at 10.30 a.m. on Saturday, December 17, 1938, in the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney.

Australasian Medical Publishing Company, Limited.

ANNUAL MEETING.

THE annual meeting of the Australasian Medical Publishing Company, Limited, was held at The Printing House, Seamer Street, Glebe, New South Wales, on November 30, 1938, Dr. T. W. Lipscomb in the chair.

Directors' Report.

The report of the directors of the company was as follows:

The directors submit their report for the twelve months ended June 30, 1938, and the balance sheet as at June 30, 1938, together with the profit and loss accounts for the twelve months ended June 30, 1938.

It is with regret that we report the death on June 12, 1938, at Brisbane, of Dr. William Nathaniel Robertson. The late Dr. Robertson was a director of the company from 1913 to 1919, and from 1920 to 1929. He was Chairman of Directors from 1923 to 1929, and during this period he did much to further the progress of the company. A bronze tablet is to be erected to his memory at The Printing House and a copy of his obituary, reprinted from THE MEDICAL JOURNAL OF AUSTRALIA and sealed in a container, is to be placed behind the tablet.

Dr. R. H. Fetherston, of Melbourne, tendered his resignation as a director on July 27, 1938, and the directors place on record their appreciation of his many years of service. Dr. Fetherston is one of the original members of the company, and has been associated with it for over twenty-five years. He was nominated as a member by the Victorian Branch Council in 1913.

We recommend that Dr. J. P. Major, of Melbourne, be appointed to fill the vacancy caused by the resignation of Dr. R. H. Fetherston.

THE MEDICAL JOURNAL OF AUSTRALIA retains its position as a scientific publication. The contributions to the journal have covered a wide range of subjects, and the standard of previous years has been maintained.

The printing and publishing department continues to turn out a large volume of work of high quality, and the plant was working at full capacity during the twelve months.

Depreciation amounting to £1,213 12s. 8d. was written off during the year, and an amount of £265 3s. 10d. has been provided for taxation. The company's reserves are used in the business, and we consider that the state of the company's affairs is satisfactory. A small surplus remains after provision has been made for the payment of debenture interest for the twelve months ended June 30, 1938.

Dr. D. Gifford Croll and Dr. A. M. Davidson retire from office by rotation in accordance with the Articles of Association (Article 39). They are eligible and present themselves for reelection.

T. W. LIPSCOMB,
Chairman.

October 18, 1938.

Election of Directors.

Dr. D. Gifford Croll and Dr. A. M. Davidson were reelected to the Board of Directors, and Dr. J. P. Major was elected in the place of Dr. R. H. Fetherston (resigned).

Post-Graduate Work.

WEEK-END COURSES AT THE PRINCE HENRY HOSPITAL, SYDNEY.

THE New South Wales Post-Graduate Committee in Medicine announces that four week-end courses will be held at the Prince Henry Hospital during 1939, as follows:

May 13 and 14: Surgery.

June 10 and 11: Electrocardiography.

August 5 and 6: Surgery.

September 9 and 10: Medicine.

Full programmes for these courses will be published later.

The fee for each course will be one guinea. Application for registration should be made (with cheque enclosed) to the Secretary, New South Wales Post-Graduate Committee in Medicine, the University of Sydney.

Obituary.

WILFRED BILLINGSLEY DIGHT.

WE regret to announce the death of Dr. Wilfred Billingsley Dight, which occurred on December 4, 1938, at Roseville, New South Wales.

Diary for the Month.

DEC. 13.—New South Wales Branch, B.M.A.: Ethics Committee.
DEC. 14.—Victorian Branch, B.M.A.: Council.
DEC. 16.—Queensland Branch, B.M.A.: Council.
DEC. 20.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments.

SIR NORMAN PAUL has been appointed a Government representative on the Board of Directors of the Sydney Hospital, Sydney, pursuant to the provisions of the *Sydney Hospital Act*, of 1881, of New South Wales.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser", pages xx to xxii.

EIDSVOLD HOSPITAL, EIDSVOLD, QUEENSLAND: Medical Officer.
CHILDREN'S HOSPITAL (INCORPORATED), PERTH, WESTERN AUSTRALIA: Junior Resident Medical Officers.
FREMANTLE HOSPITAL, FREMANTLE, WESTERN AUSTRALIA: Junior Resident Medical Officer.
LAUNCESTON GENERAL HOSPITAL, LAUNCESTON, TASMANIA: Junior Resident Medical Officers.
NATIONAL HOSPITAL, QUEEN SQUARE, LONDON, ENGLAND: Research Fellowship.
ORANGE BASE HOSPITAL, ORANGE, NEW SOUTH WALES: Resident Medical Officers.
ROYAL HOBART HOSPITAL, HOBART, TASMANIA: Resident Medical Officers.
VICTORIAN EYE AND EAR HOSPITAL, MELBOURNE, VICTORIA: Resident Surgeons.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCHES.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17.	Brisbane Associate Friendly Societies' Medical Institute. Proserpine District Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 178, North Terrace, Adelaide.	All Lodge appointments in South Australia. All contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.

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